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La sténose du tronc commun coronaire gauche. Résultats immédiat et à moyen terme du pontage aorto-coronaire

Acute and mid-term results of coronary artery bypass grafting for unprotected left main coronary artery disease

Ben Ahmed Habib, El Kateb Taoufik ,Boussaid Houssem,El fazaa Samia ,Mokkadem Aida ,Ben Ameur Youssef, Longo Salma, Boujnah Mohamed Rachid

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Résumé

Pré-requis : La sténose du tronc commun gauche est la plus sévère des lésions coronaires. Le pontage aortocoronaire représente le traitement de référence des sténoses du tronc commun gauche non protégé.
But : analyser les résultats immédiats et à moyen terme de la revascularisation chirurgicale des sténoses du tronc commun coronaire gauche.
Patients et Méthodes : C'est une étude rétrospective portant sur 100 patients atteints d'une sténose du tronc commun gauche non protégé, ayant bénéficié d'une chirurgie de pontage aortocoronaire entre Janvier 2006 et Avril 2011.
Résultats : L'âge moyen des patients était de 63,02 ± 9,4 ans avec une nette prédominance masculine (82%). L'HTA et le tabac représentaient les facteurs de risque les plus fréquents, et un patient sur deux était diabétique. La sténose du tronc commun gauche était distale dans 63% des cas, une atteinte tritronculaire associée était retrouvée chez 55 patients, et la fraction d'éjection ventriculaire gauche moyenne était 56,6 ± 13,4%. Un total de 309 pontages ont été réalisés soit en moyenne 3,09 ± 0,72 pontages par patient. La revascularisation a été totalement artérielle chez seulement 28 patients et la cardioplégie antérograde était l'unique moyen de protection myocardique. Le taux de mortalité post opératoire était de 15%, le taux d'événements cardiaques majeurs à un an était de 17,65% avec une mortalité de 5,9%. Les facteurs prédictifs de mortalité hospitalière en analyse multi variée étaient :le diabète, un âge supérieur à 70ans, et un L'Euro score supérieur ou égal à 7. Les facteurs prédictifs indépendants de survenue d'événements cardiaques majeurs à un an étaient : le tabac et une fraction d'éjection ventriculaire gauche inférieure à 50%.
Conclusion: Cette série retrouve une mortalité postopératoire très importante qui semble être en rapport avec le profil clinique sévère des patients et le mode de protection myocardique peropératoire. Le taux d'événements cardiaques majeurs à moyen terme reste comparable à celui rapporté dans la littérature.

Mots-clés
Le tronc commun coronaire gauche, pontage aortocoronaire

Summary

Background : Significant left main coronary artery disease is associated with poor prognosis when medically treated. For unprotected left main stenosis, coronary artery bypass grafting is still regarded as the "standard of care" in an era of growing interest in LMS stenting.
Aim : The purpose of this study was to analyze short and mid-term follow-up after coronary artery bypass grafting for significant left main stenosis.
Patients and Methods: We evaluated 100 patients with unprotected left main coronary artery disease who underwent coronary artery bypass grafting between January, 2006 and April, 2011.
Results :The mean age was 63,02 ± 9,4 years. High blood pressure and smoking represented the most frequent cardiovascular risk factors, and 48% of patients were found to have diabetes. The LMS was distal in 63 % of the cases, 55 patients had multivessel disease associated to LMS, and the mean left ventricular ejection fraction was 56.6 ± 13.4 %. A total of 309 bypasses were realized with an average of 3.09 ± 0.72 bypasses by patient.
Total arterial revascularization was performed only for 28 patients and only antegrade cardioplegia was performed for all patients. In-hospital mortality was 15 %. At 1 year, the rate of major adverse cardiac events was 17.65% and the 1-year incidence was 5.9% for all-cause mortality. The main risk factors of in- hospital mortality were diabetes mellitus, age > 70 years and Euroscore ≥ 7. Multivariate analysis suggests that smoking and low left ventricular ejection fraction (<50%) were significant predictors of major adverse cardiac events.
Conclusion : In our study, the rate of major adverse cardiac events remains comparable to that reported in the literature but we found a higher incidence of in-hospital mortality which seems caused by the high surgical risk of the patients treated and the modalities of myocardial protection during cardiac surgery.

Keywords
Left main coronary artery, Coronary artery bypass grafting

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INTRODUCTION

La sténose du tronc commun gauche (TCG) est la plus sévère des lésions coronaires en raison du grand territoire myocardique concerné par l'ischémie mettant en jeu le pronostic vital.
Une lésion significative (> 50 % par rapport au diamètre de référence) du tronc commun est retrouvée dans 3 à 7 % des angiographies coronaires pathologiques et elle est souvent associée à une atteinte pluri tronculaire (1).
L'histoire naturelle de cette localisation particulière de la maladie athéromateuse a été décrite dans les années 1970 : pronostic spontané sombre avec une mortalité à 5 ans de 50 %(1,2).Dans la même période, l'étude CASS a confirmé le bénéfice indiscutable de la chirurgie de pontage aorto coronaire (PAC), comparé au traitement médical en terme de survie des patients atteints d'une sténose du tronc commun. Le traitement chirurgical est devenu alors le traitement de référence (3).
Nous nous proposons dans ce travail d'analyser les résultats immédiats et à moyen terme de la revascularisation chirurgicale des sténoses du tronc commun coronaire gauche.

PATIENTS ET MÉTHODES

C'est une étude rétrospective portant sur 100 patients atteints d'une sténose du TCG non protégé, ayant bénéficié d'une revascularisation myocardique chirurgicale entre Janvier 2006 et Avril 2011.
Les patients avec des antécédents de PAC ou d'Angioplastie du TCG et ceux aux antécédents de chirurgie cardiaque à cœur ouvert ont été exclus.
Les résultats et les complications postopératoires ont été relevés .Nous avons procédé par ailleurs à un suivi clinique de 12 mois. Les événements majeurs (MACCE): Décès, syndrome coronarien aigu sans sus décalage du segment ST(SCA ST(-)),syndrome coronarien aigu avec sus décalage du segment ST(SCA ST(+)), AVC, Insuffisance cardiaque et le moment de leur survenue ont été étudiés. Les données ont été saisies et analysées au moyen du logiciel SPSS version 18.
Nous avons calculé des fréquences simples et des fréquences relatives pour les variables qualitatives. Nous avons calculé des moyennes, des médianes et des écarts-types (déviations standard) et déterminé l'étendue pour les variables quantitatives.
Les comparaisons de 2 moyennes sur séries indépendantes ont été effectuées au moyen du test « t » de « Student » pour séries indépendantes, et en cas de faibles effectifs par le test non paramétrique de « Mann et Whitney ».
Afin d'identifier les facteurs de risque directement liés à l'événement, nous avons conduit une analyse multi variée en régression logistique.

RÉSULTATS

L'âge moyen des patients était de 63,02 ± 9,4 ans avec une nette prédominance masculine (82%). Il s'agit d'une population à haut risque cardiovasculaire puisque 31% avaient au moins 3 facteurs de risque. L'HTA et le tabac représentaient les facteurs de risque les plus fréquents, et un patient sur deux était diabétique (Tableau 1).

Tableau 1 : les caractéristiques cliniques de la population.

Effectif	100 patients
Âge moyen	63,02 ± 9,4 ans
Sexe Féminin	18 (18%)
HTA	60 (60%)
Diabète	48 (48%)
Tabac	64 (64%)
Dyslipidémie	33 (33%)
IMC	26,35 ± 4 ,06
STEMI	20 (20%)
NSTEMI	10 (10%)
Angor instable	32 (32%)
Angor stable	38 (38%)
IRC	3 (3%)
BPCO	4 (4%)
Antécédent AVC	10 (10%)
AOMI	10 (10%)

AVC : accident vasculaire cérébral, STEMI :infarctus du myocarde avec sus décalage de ST,NSTEMI :infarctus du myocarde sans sus décalage de ST ,AOMI : artériopathie oblitérante des membres inferieurs, BPCO : bronchopneumopathie chronique obstructive.

La sténose du TCG était distale dans 63% des cas, une atteinte tritronculaire associée était retrouvée chez 55 patients, et la fraction d'éjection ventriculaire gauche (FEVG) moyenne était 56,6 ± 13,4%(Tableau II).Le délai médian entre la coronarographie et la chirurgie était de 15,13 jours.

Tableau 2 : Caractéristiques angiographiques et Euroscore

	100 patients
TCG ostial	25 (25%)
TCG médian	5 (5%)
TCG distal	63 (63%)
Sténose diffuse	7 (7%)
TCG isolé	1 (1%)
TCG + 1 Vaisseau	10 (10%)
TCG +2 Vaisseaux	34 (34%)
TCG +3 Vaisseaux	55 (55%)
TCG + sténose CD	65 (65 %)
FE VG	56,6 ± 13,4%
Euroscore moyen	3,8 ± 2,7
Euroscore ≥ 7	26 (26%)

Au total, 309 pontages ont été réalisés soit en moyenne 3,09 ± 0,72 pontages par patient (Tableau III).
La revascularisation a été totalement artérielle chez seulement 28 patients et 10 patients ont bénéficié d'un

geste associé (6 endartériectomies, 3 plasties mitrales et 1remplacement valvulaire aortique).

Tableau 3 : les caractéristiques des procédures de revascularisation chirurgicale

	Effectif
Mono pontage	5
Double pontage	19
Triple pontage	41
Quadruple pontage	34
Quintuple pontage	1
Revascularisation en tout artériel	28
Revascularisation en tout veineux	4
Utilisation d'un greffon radial	2
Pontages séquentiels	39
Nombre de greffons sur l'I.V.A	99
Nombre de pontages avec geste associé	10
Revascularisation à cœur battant	2
Durée moyenne du clampage	63,4mn ± 23,39mn
Durée moyenne de la C.E.C	94,3mn ± 33,16mn

La sortie de la circulation extracorporelle (CEC) a été sous inotropes positifs chez 31 patients et le recours à un ballon de contre pulsion intra aortique (BCPIA) a été nécessaire chez 3 patients.
La mortalité post opératoire était de 15% (15 patients) et les complications non fatales sont résumées dans le tableau IV.

Tableau 4 : Complications post opératoires et causes des décès

Population	100 patients
causes des décès post opératoires	15
état de choc cardiogénique	8
état de choc septique	3
état de choc hémorragique	1
troubles du rythme ventriculaire	1
Cause de décès non précisée	2
Complications non fatales	17
Médiastinite	2
Infection pleuro pulmonaire	7
Hémorragie nécessitant une reprise	2
Embolie Pulmonaire	1
AVC ischémique	1
Insuffisance rénale nécessitant la dialyse	2
Syndrome de bas débit	2

Les facteurs prédictifs indépendants de mortalité hospitalière en analyse multi variée étaient : Le diabète, un âge supérieur à 70ans, L'Euro score supérieur ou égal à 7.
Après un suivi de 12mois, 15 patients (17,65%) ont présenté des événements majeurs (MACCE) dont 5 décès (5,89%) et 10 évènements majeurs non fatals (11,67%). La survie sans événements à un an était de 83 % (figure 1).

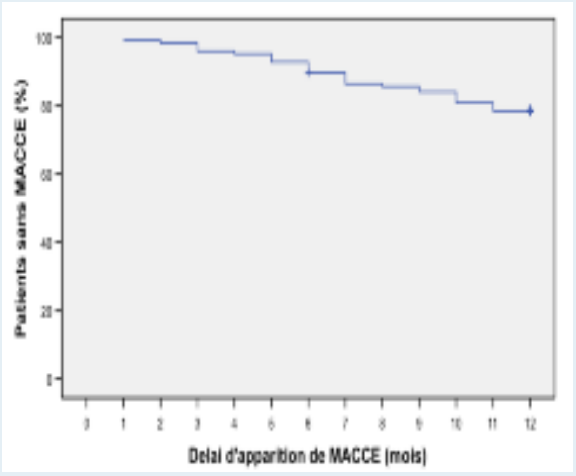

Figure 1 : Courbe d'événements majeurs MACCE après 12 mois de suivi, la survie sans événements à un an était de 83 %.

La répartition des MACCE au cours du suivi selon le type de la complication est présentée dans le tableau V.

Tableau 5 : Résumé des MACCE après un suivi de 12 mois.

MACCE	Effectif	Pourcentage/population
Total de MACE	15	17.65%
Décès	5	5.7%
STEMI	3	3,6%
NSTEMI	2	2.4%
Angor instable	2	2.4%
Angor d'effort	1	1.2%
I.Cardiaque	2	2.4%

En analyse uni variée, les facteurs prédictifs de survenu de MACCE à moyen terme sont : l'hérédité coronaire, le tabagisme, Le siège distal de la lésion du tronc commun gauche, une FEVG inférieure à 50%.
Les facteurs indépendants prédictifs de survenue de MACCE a un an en analyse multi variée sont : le tabac, une FEVG inférieure à 50% (tableau VI).

Tableau 6 : Facteurs prédictifs de mortalité hospitalière et de MACCE à 1 an

Mortalité postopératoire	IC (95%)	OR ajusté	P
Age >70ans			
Diabète	1,406-62,083	9,432	0,021
EURO score ≥7	1,475-69,422	10,120	0,018
MACE à 1an	1,345-54,156	7,423	0,035
Tabagisme	IC (95%)	OR ajusté	P
FEVG < à 50%.	-1,315 – 0,667	0,268	0,049
	-1,562 - 0,715	0,210	0,029

DISCUSSION

Dans cette étude le taux de mortalité hospitalière était élevé (15%), la mortalité à un 12 mois était de 5,9% avec un taux de survie sans événements de 83 %.
Le pontage aortocoronaire représente le traitement de référence des sténoses du TCG(4).
Les séries récentes consacrées à la chirurgie des lésions du TCG ont retrouvé une mortalité hospitalière de 2.8% et une mortalité à 30 jours entre 3 et 4.2% (5-7).
Cependant ces résultats sont fortement influencés par la présence de comorbidité comme il a était bien démontré dans l'étude d'Ellis (7) ou la mortalité à 3ans de la chirurgie du TCG variait de 4% chez les malades à faible risque à 40% chez les patients avec une lourde comorbidité (8 - 11).
Le registre de la société britannique de chirurgie cardiothoracique englobant 5003 patients avec une sténose du TCG trouve une mortalité postopératoire de 3%, ce taux est inférieure à 2% chez plus de 17000 patients sans atteinte du TCG du même registre, la survie à 2ans était de 94% (11).
Dans notre série, nous avons révélé un taux très élevé de mortalité post opératoire avec 15% de décès. Cette mortalité excessive pourrait être expliquée en partie par la sévérité des caractéristiques cliniques des patients et par la technique utilisée pour la protection myocardique.
Dans cette série nous avons enregistré les taux de tabagique et de diabétiques les plus élevés en comparaison avec des travaux similaires. En effet 48,8% des patients étaient diabétiques comparés aux 14,4% retrouvés dans la série de Lu et al (6) et aux 19% de l'étude de Murzi (5) et 64,8% sont tabagiques par rapport aux 17% de la série de Lu (6).
Le tabac constitue un facteur aggravant le pronostic post opératoire par le biais de l'hypoxie, les problèmes de réveil de l'anesthésie et par son rôle favorisant la surinfection bronchique.
En outre, une proportion non négligeable de ces fumeurs actifs regroupait très probablement des bronchitiques chroniques non diagnostiqués et qu'on n'a pas eu le temps de les évaluer et de les préparer sur le plan respiratoire avant la chirurgie dans ce contexte de sténose du TCG.
Dans cette série le diabète constitue un facteur prédictif indépendant de mortalité hospitalière. C'est un facteur aggravant le pronostic par le biais des infections médiastinales et pulmonaires ainsi que par les troubles métaboliques qu'il génère. Plusieurs études ont retrouvé cette surmortalité post opératoire liée au diabète comme celle de Murzi (5) et d'Ellis (7) où le diabète était prédictif de décès au décours d'une revascularisation chirurgicale du TCG.
A coté du diabète, l'âge supérieur à 70 ans et l'EURO score supérieur à 7 étaient des facteurs prédictifs indépendant de mortalité post opératoire.
Cela rejoint les résultats de la littérature. En effet et d'une part, l'âge avancé a été individualisé comme un facteur prédictif (5- 7).D'autre part, plusieurs autres facteurs ont été associés à une surmortalité hospitalière dans plusieurs études telle que l'insuffisance rénale chronique dans l'étude d'Ellis (7) et l'instabilité hémodynamique pré opératoire dans la série de Murzi (5). Ces facteurs ne sont au fait que les composantes de l'EURO score qui a été corrélé à une surmortalité hospitalière dans notre travail.
Rappelons que le risque opératoire de notre population était sous-estimée par l'EURO score I adopté dans cette étude. L'utilisation de l'EURO score II qui intègre le diabète reflète mieux le niveau de risque de ces patients à forte prédominance diabétique.
En fin, la découverte de la sténose du tronc était fréquemment au décours d'un syndrome coronarien aigu, dont on connait l'impact pronostique.
Par ailleurs, la qualité de la protection myocardique conditionne le pronostic post opératoire. En effet, La solution de cardioplégie doit fournir au cœur les éléments de sa survie jusqu'à la reprise de son activité. Elle doit préserver ses réserves d'ATP, réduire le métabolisme anaérobique, et prévenir la formation de radicaux libres et la surcharge calcique à la reperfusion.
Dans notre série, la cardioplégie était antérograde à travers une sténose du tronc commun chez tous les patients. Une protection myocardique optimale était difficile à réaliser dans ces conditions puisqu'en cas de sténose coronarienne proximale serrée, a fortiori en présence d'une sténose serrée du TCG, le débit distal du perfusât est compromis. De même, la perfusion sous-endocardique est réduite lorsque le ventricule fibrille.
Ces caractéristiques expliquent en partie la morbi-mortalité élevée après le pontage aorto coronaire.
Une perfusion rétrograde de la solution de cardioplégie par le sinus coronaire permet d'obtenir une protection myocardique homogène dans le territoire des coronaires sténosées .Par ailleurs une stratégie combinée avec une association des deux voix de perfusion rétrograde et antérograde peut etre proposée pour assurer une cardioprotection optimale. En pratique, ces méthodes sont rarement utilisées en Tunisie et la voie la plus fréquemment adoptée demeure la voie antérograde classique.
Nous avons constaté par ailleurs des taux de complications post opératoires comparables avec la littérature en dehors des infections pulmonaires qui ont été supérieures avec 8,3% comparés aux 5% retrouvés dans l'étude de Lu (6). Cela est expliqué par le taux important de diabétiques et de tabagiques dans notre série.
Le suivi à 1 an a révélé un taux de mortalité de 5,9%, ce taux est similaire a ceux retrouvés dans la

littérature(8,9). En effet il était de 5% dans l'étude de Lu (6) et de 4,5% dans le sous groupe « TCG » de l'étude SYNTAX (12).
Le taux de MACCE dans notre série était de 17,6% avec 11,7% d'évènements non fatals, l'analyse multi variée retient la dysfonction systolique du VG et le tabac comme facteurs prédictifs de survenue d'évènements majeurs. Ce fléau favorise la progression de la maladie athéromateuse au niveau des ponts mais surtout au sein du réseau coronaire natif. Cela a été démontré dans notre travail puisque 60% des patients ayant présenté des évènements non fatals ont présenté des récidives angineuses en rapport avec une progression des lésions athéromateuse sur le réseau natif dans 40% des cas.

L'avènement des stents actifs, l'amélioration de l'environnement pharmacologique péri procédural avec l'apparition de protocoles antiplaquettaires sécurisants et l'expérience grandissante des opérateurs ont permis de démystifier l'angioplastie du TCG et a proposer cette dernière comme alternative thérapeutique pour des malades bien sélectionnés. Parallèlement au progrès réalisé en cardiologie interventionnelle, Les techniques de revascularisation chirurgicale se sont aussi améliorées avec le développement de techniques moins invasives, les techniques du « no-touch aortique », du cœur battant, de la revascularisation artérielle complète et de l'amélioration de la qualité de la réanimation post opératoire. Ces progrès réalisés dans les deux techniques de revascularisation chirurgicales et percutanées contribueront sans doute a diminuer la morbi-mortalité des patients atteints de sténose du TCG.

Limites de l'étude :

Les principales limites de ce travail sont représentées par le caractère rétrospectif de l'étude et son faible effectif. Les patients ont été opérés par plusieurs équipes avec des niveaux d'expertise différents. Enfin, le suivi à douze mois reste insuffisant pour tirer des conclusions fiables.

CONCLUSION

Le pontage aortocoronaire reste « le gold standard » dans la prise en charge des lésions du TCG non protégé. Cette série retrouve une mortalité postopératoire très importante, très probablement en rapport avec le profil clinique sévère des patients et le mode de protection myocardique peropératoire. En effet notre population s'est distinguée par un taux très élevé de diabétiques, par les circonstances de découverte de l'atteinte du TCG qui était souvent au décours d'un SCA et par une cardioplégie antérograde qui reste insuffisante en présence de sténose sévère du TCG.
Le taux d'événements majeurs (MACE) à moyen terme reste cependant comparable à celui rapporté dans la littérature.

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Summary

Important advances have been made in the past few years in the fields of clinical cardiac electrophysiology and pacing. Researchers and clinicians have a greater understanding of the pathophysiological mechanisms underlying atrial fibrillation (AF), which has transpired into improved methods of detection, risk stratification, and treatments. The introduction of novel oral anticoagulants has provided clinicians with alternative options in managing patients with AF at moderate to high thromboembolic risk and further data has been emerging on the use of catheter ablation for the treatment of symptomatic AF. Another area of intense research in the field of cardiac arrhythmias and pacing is in the use of cardiac resynchronisation therapy (CRT) for the treatment of patients with heart failure. Following the publication of major landmark randomised controlled trials reporting that CRT confers a survival advantage in patients with severe heart failure and improves symptoms, many subsequent studies have been performed to further refine the selection of patients for CRT and determine the clinical characteristics associated with a favourable response. The field of sudden cardiac death and implantable cardioverter defibrillators also continues to be actively researched, with important new epidemiological and clinical data emerging on improved methods for patient selection, risk stratification, and management. This review covers the major recent advances in these areas related to cardiac arrhythmias and pacing.

ATRIAL FIBRILLATION

Epidemiology of atrial fibrillation

A number of large scale epidemiological studies using registry databases and prospective cohort data have reported novel associations between atrial fibrillation (AF) and other non-traditional risk factors for AF. These include an increased risk of incident AF in patients with high glycosylated haemoglobin (HbA1c) and poor glycaemic control,[1] coeliac disease,[2] rheumatoid arthritis[3] and psoriasis,[4] use of non-aspirin, non-steroidal anti- inflammatory drugs (NSAIDs),[5] and increased height.[6] Another interesting association is the finding from a substudy of 260 patients with chronic AF from the SAFETY trial (Standard versus Atrial Fibrillation Specific Management Study) that mild cognitive impairment is highly prevalent among older, high risk patients hospitalised with AF.[7] In another substudy of the Cardiovascular Health Study, investigators found that higher base- line circulating concentrations of total long chain n-3 polyunsaturated fatty acids (PUFA) were associated with a lower risk of incident AF.[8]

Other interesting recent epidemiological studies on AF include the association of incident AF with an increased risk of developing end stage renal disease in patients with chronic kidney disease,[9] and a community based study of 3220 patients which showed that new AF in patients with no history of AF before a myocardial infarction increased mortality in patients with myocardial infarction.[10] In a large Swedish registry study of 100 802 patients with AF, Friberg et al[11] found that ischaemic strokes were more common in women than in men, supporting the notion that female gender should be taken into consideration when making decisions about anticoagulation treat- ment. Furthermore, among older

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patients admitted with recently diagnosed AF, the risk of stroke appears to be greater in women than in men, regardless of warfarin use,[12] and among healthy women new onset AF was found to be independ- ently associated with all cause cardiovascular and non-cardiovascular mortality.[13]

Medical management of AF

Data from the RealiseAF study, an international, observational, cross-sectional survey of patients with any history of AF in the previous year, sug- gested that patients in which their AF was 'con- trolled' (defined as sinus rhythm or AF with a resting heart rate ≤80 beats/min) had a better quality of life and fewer symptoms than those whose AF was uncontrolled.[14] Nonetheless, even patients with controlled AF experienced frequent symptoms, functional impairment, altered quality of life and cardiovascular events—hence the importance of ongoing efforts to develop novel and better treatments for AF. The RECORDAF (Registry on Cardiac Rhythm Disorders Assessing the Control of Atrial Fibrillation) registry was a worldwide, prospective observational survey of AF management in an unselected, community based cohort over a 12 months period.[15] The investiga- tors found that in 5171 patients whose data were available, therapeutic success (driven by control of AF) was achieved in 54% overall (rhythm control 60% vs rate control 47%). The choice of rate or rhythm strategy did not affect clinical outcomes (which were driven mainly by hospitalisations for arrhythmia and other cardiovascular causes), although the choice of rhythm control reduced the likelihood of AF progression. The RACE (Rate Control Efficacy in Permanent Atrial Fibrillation) II trial was the first formal assessment of alternative rate control goals in AF and demon- strated for the first time that a 'lenient rate control' strategy (target resting heart rate <110 beats/min) was non-inferior to a 'strict rate control' strategy (target resting heart rate <80 beats/ min and heart rate during moderate exercise <110 beats/min).[16] Two subsequent sub-studies of the RACE II trial showed that the stringency of rate control had no significant effect on the quality of life in patients with permanent AF[17] and that lenient rate control did not have an adverse effect on atrial and ventricular remodelling compared with strict rate control (although female gender was independently associated with significant adverse cardiac remodelling).[18] In another sub-study looking at cardio- vascular outcomes in subjects from the original AFFIRM trial (Atrial Fibrillation Follow-Up Investigation of Rhythm Management), investigators found that the composite outcome of mortality or cardiovascular hospital stays was better in rate compared with rhythm control strategies (using amiodarone or sotalol).[19] Non- cardiovascular death and intensive care unit hos- pital stay were more frequent in patients on amiodarone, and time to cardiovascular hospital stay was shorter. In a prospective, randomised, open label trial of pharmacological cardiover- sion in patients with persistent AF, Yamase et al compared amiodarone with bepridil in 40 consecutive subjects.[20] The investigators found that bepridil was superior to amiodarone in achieving sinus conversion (85% vs 35%; $p<0.05$) and main- taining sinus rhythm after an average follow-up of 14.7 months (75% vs 50%).

The issue of whether PUFA have any beneficial effects on AF remains a topical one. A large meta-analysis of 10 randomised controlled trials involving 1955 patients found that PUFA supple- mentation had no significant effect on AF prevention.[21] In the FORWARD trial (Randomised Trial to Assess Efficacy of PUFA for the Maintenance of Sinus Rhythm in Persistent Atrial Fibrillation), 586 outpatient participants with confirmed symp- tomatic paroxysmal AF who required cardioversion or had at least two episodes of AF in the preceding 6 months were randomly assigned to receive placebo or PUFA (1 g/day) for 12 months.[22] The investigators found that PUFA supplementation did not reduce the recurrence of AF or have any beneficial effects on the other prespecified end points (all cause mortality, non- fatal stroke, non-fatal acute myocardial infarction, systemic embolism or heart failure). In a large placebo controlled, randomised clinical trial involving 1516 patients in 28 centres, perioperative supplementa- tion of PUFA, although well tolerated, was not shown to reduce the risk of postoperative AF.[23] In contrast, another randomised, double blind, placebo controlled trial involving 199 patients who received either PUFA (2 g/day) or placebo for 4 weeks before direct current (DC) cardioversion found that patients who received PUFA were more likely to be in sinus rhythm at 1 year follow- up compared with control patients.[24]

Monitoring and assessment of AF

The detection of paroxysmal AF can be difficult with current methods and technology; hence ongoing efforts are being made to improve methods for detection and diagnosis. The associ- ation between subclinical AF and cryptogenic stroke has gained increasing prominence with more careful monitoring of patients using invasive and non-invasive methods. In a nice study of 2580 patients aged 65 years or older with a pacemaker or

defib- rillator recently implanted and no history of AF, investigators detected subclinical atrial tachyarrhythmias in 261 patients (10.1%).[25] Over a mean follow-up of 2.5 years, patients with subclinical atrial tachyarrhythmias were found to have an increased risk of clinical AF and of ischaemic stroke or systemic embolism (HR 2.49, 95% CI 1.28 to 4.85; p=0.007). In patients who do not have pacemakers or defibrillators who present with cryptogenic stroke, longer term ambulatory ECG monitoring using external or implantable devices may be worth considering to help confirm a diagnosis of subclinical AF.[26 27] In a study of 100 patients being screened for AF, investigators com- pared the effectiveness of using 7-day triggered ECG monitor- ing with 7-day continuous Holter ECG monitoring for detection of AF.[28] An arrhythmia was recorded in 42 subjects (42%) with continuous ECG recordings versus 37 subjects (32%) with triggered monitoring (p=0.56). The sensitivity of triggered ECG monitoring was found to be lower than that of continuous ECG monitoring, mainly due to a shorter effective monitoring duration, although qualitative triggered ECG ana- lysis was less time consuming than continuous ECG analysis. In another larger study of 647 patients with implantable continu- ous monitoring devices, intermittent rhythm monitoring was found to be significantly inferior to continuous monitoring for the detection of AF and was not able to identify AF recurrence in a great proportion of patients at risk.[29] In an interesting study investigating the use of N-terminal pro B-type natriuretic peptide (NT-proBNP) values to estimate the recency of AF onset and safety of cardioversion, investigators separated 86 patients presenting with presumed recent onset AF into two groups (43 in each group), based on NTproBNP concentrations above and below a cut-off value, and subjected all subjects to transoesopha- geal echocardiography.[30] NT-proBNP concentrations below the cut-off value were found to be the most powerful predictor of the presence of thrombus, suggesting that a short term increase in NT-proBNP after AF onset might be useful in assessing the recency of onset of the AF episode, if unknown, and might be potentially used to help determine the safety of cardioversion.

Catheter ablation of AF

Although antiarrhythmic drugs (AADs) and catheter ablation are the main treatment options available to maintain sinus rhythm in symptomatic patients with AF, many clinicians and patients still opt for an initial conservative strategy and consider catheter ablation only after one or more AADs have been tried and found to be ineffective. The question of whether catheter abla- tion of AF is an effective initial therapy for paroxysmal AF was addressed in a small randomised study in which 294 patients (with no history of AAD use) were randomly assigned to an initial strategy with radiofrequency catheter ablation or therapy with a class 1c or III AAD.[31] The investigators found no signifi- cant difference between the ablation and drug therapy groups in the cumulative burden of AF (90th centile of arrhythmia burden 13% and 19%, respectively; p=0.10) in the initial 18 months. However, at 24 months, AF burden was significantly lower in the ablation group compared with the drug therapy group (9% vs 18%; p=0.007) and more patients in the ablation group were free from symptomatic AF (93% vs 84%; p=0.01). In the drug therapy group, 54 patients (36%) subsequently underwent ablation.

In another small randomised study of AF ablation in patients with persistent AF, advanced heart failure and severe left ven- tricular (LV) systolic dysfunction, MacDonald et al[32] found that catheter ablation was successful at restoring sinus rhythm in 50% of patients, although the procedure was associated with a significant complication rate of 15%. In addition, catheter abla- tion did not improve LV ejection fraction (LVEF) (as measured using cardiovascular magnetic resonance) or other secondary outcomes, calling into question the risk/benefit ratio of perform- ing AF ablation in patients with persistent AF and LV dysfunction. An international multicentre registry study of 1273 patients undergoing AF ablation suggested that maintenance of sinus rhythm through catheter ablation was associated with a lower risk of stroke and death compared with a control group consisting of medically treated patients with AF in the Euro Heart Survey.[33]

Several studies have recently been reported which increase our understanding of the factors associated with success or failure following AF ablation. The importance of pulmonary vein (PV) isolation was further reinforced by Miyazaki et al[34] who reported long term clinic outcomes of 83.6% (480 out of 574 patients) with a mean follow-up of 27±14 months using an extensive PV isolation approach in patients with both paroxys- mal and persistent AF.[34] Late recurrences (defined as 6-12 months following the initial AF ablation procedure) was asso- ciated with PV reconnection in all patients, while very late recurrences (>12 months after the procedure) were associated with non-PV triggers in 85.7% of cases. The added benefit of performing additional linear ablation lines after PV isolation on improving outcomes following AF ablation has been

further questioned in a prospective, randomised study of 156 patients with paroxysmal AF who were randomly assigned to undergo PV isolation only, PV isolation and a roof line, or PV isolation, roof line and a posterior inferior line.[35] The investigators found no improvement in clinical outcome in the patients who received the additional lines while, unsurprisingly, the addition of the linear ablations significantly prolonged procedure times.
A number of investigators have found that many factors are pre- dictive of or adversely related to outcome following AF ablation in addition to well established factors, such as type of AF (par- oxysmal or persistent), left atrial size, and presence of LV dysfunction. These novel factors include cardiac related factors, such as atrial electromechanical interval on pulse wave Doppler imaging[36] and left atrial fibrosis as assessed by measuring echo- cardiograph derived calibrated integrated backscatter,[37] pericar- dial fat,[38] plasma biomarkers (such as plasma B-type natriuretic peptide values[39]), renal dysfunction,[40] and the metabolic syn- drome.[41]
Interestingly, the presence of dissociated PV potentials, often used as a marker of successful PV isolation, was not found to predict AF recurrence in a study of 89 consecutive patients over a mean follow-up of 21±8 months.[42] In a small rando- mised controlled study of 161 patients, a 3 month course of col- chicine (0.5 mg twice daily) was found to decrease early AF recurrence after PV isolation, probably due to a reduction in inflammatory mediators, including interleukin 6 (IL-6) and C reactive protein (CRP).[43] Colchicine (1.0 mg twice daily initially followed by a maintenance dose of 0.5 mg twice daily for 1 month) was also found to reduce the incidence of post- operative AF and decrease in-hospital stay in a multicentre, double blind, randomised trial of 336 patients.[44] In an interest- ing small randomised study of PV isolation with and without concomitant renal artery denervation in 27 patients with refrac- tory symptomatic AF and resistant hypertension, Pokushalov et al showed that renal artery denervation reduced systolic and diastolic blood pressure and reduced the recurrence of AF during 1 year follow-up.[45]
Another area of research in the field of AF ablation has been on the factors associated with increased complications from the procedure. Using data from the California State Inpatient Database, Shah et al found that among 4156 patients who underwent an initial AF ablation procedure, 5% had periproce- dural complications (most commonly vascular) and 9% were readmitted within 30 days.[46] Factors associated with a higher risk of complications and/or 30-day readmission following an AF ablation were older age, female sex, prior AF hospitalisa- tions, and recent hospital procedure experience. In another retrospective study of 565 patients, both the $CHADS_2$ and CHA_2DS_2-VASc scores were found to be useful predictors of adverse events following AF ablation.[47]
The first randomised clinical trial comparing the efficacy and safety of catheter ablation of AF with surgical ablation involved 124 patients with drug refractory AF.[48] The investigators found that the primary end point (freedom from left atrial arrhythmia>30 s without AADs after 12 months) was 36.5% for the cath- eter ablation group and 65.6% for the surgical group (p=0.0022), but patients in the surgical group experienced significantly greater adverse effects (driven mainly by procedural complications) compared to the catheter ablation group. Pison et al reported relatively high 1 year success rates (93% for par- oxysmal AF and 90% for persistent AF) with a combined trans- venous endocardial and thorascopic epicardial approach for a single AF ablation procedure in a small cohort of 26 patients with AF.[49]

Strategies to decrease thromboembolism

The use of novel oral anticoagulants to decrease the risk of stroke and systemic thromboembolism in patients with AF has gained increasing use and acceptance over the past several years following the publication of a number of landmark multicentre, randomised clinical trials comparing their efficacy with conven- tional vitamin K antagonists.[50-53] A meta-analysis of 12 studies totalling 54 875 patients showed a significant reduction of intra-cranial haemorrhage with these novel anticoagulants compared with vitamin K antagonists, and a trend toward reduced major bleeding.[54] These novel oral anticoagulants may also have a role in patients undergoing DC cardioversion. A sub-study of patients with AF who underwent cardioversion in the RE-LY (Randomised Evaluation of Long-Term Anticoagulation Therapy) trial showed that dabigatran (at two doses of 110 and 150 mg twice daily) is a reasonable alternative to warfarin, with low frequencies of stroke and major bleeding within 30 days of cardioversion.[55]
These novel oral anticoagulants may also have a role to play in the periprocedural anticoagulation of patients undergoing radiofrequency ablation for AF. Several registry and observa- tional studies have suggested that dabigatran is as safe as peri- procedural warfarin in patients undergoing AF ablation,[56-58] although one study suggested an increased risk of bleeding and thromboembolic complications with dabigatran compared with warfarin.[59] A prospective randomised

controlled trial is required to definitively address the issue as to whether these novel oral anticoagulants can be used in place of warfarin for periproce- dural anticoagulation in patients undergoing AF ablation. Economic evaluation of these novel oral anticoagulants suggest that they may be cost effective as a first line treatment for the prevention of stroke and systemic embolism,[60] especially in patients at high risk of haemorrhage or stroke, unless inter- national normalised ratio (INR) control with warfarin is already excellent.[61]

Another strategy to decrease thromboembolic events in patients with AF that is gaining favour involves the use of mech- anical left atrial appendage (LAA) occlusion devices. In a system- atic review of 14 studies, implantation of LAA occlusion devices in patients with AF was successful in 93% of cases, with peri- procedural mortality and stroke rates of 1.1% and 0.6%, respectively; the overall incidence of stroke among all studies was 1.4% per annum.[62] A substudy of the PROTECT AF (Percutaneous Closure of the LAA versus Warfarin Therapy for Prevention of Stroke in Patients with AF) study reported that 32% of implanted patients had some degree of peri-device flow at 12 months on transoesophageal echocardiography, although this did not appear to be associated with an increased risk of thromboembolism compared to patients with no peri-device flow who discontinued warfarin.[63] A systematic review aimed at determining which subgroups of patients would benefit most from LAA closure devices looked at the location of atrial thrombi in patients with AF in a total of 34 studies.[64] The inves- tigators concluded that patients with non-valvular AF may derive greater benefit from LAA closure devices—56% of patients with valvular AF had atrial thrombi located outside the LAA, 22% in mixed cohorts and 11% in non-valvular AF patients.

CARDIAC RESYNCHRONISATION THERAPY AND PACING

Cardiac resynchronisation therapy

Recent research in the area of cardiac resynchronisation therapy (CRT) has looked at the long term effects of CRT pacing on LV and right ventricular (RV) function and further into which sub- groups of patients may derive greatest benefit from CRT pacing. A favourable RV functional response to CRT appears to be associated with improved survival in patients with CRT devices, and RV function was found to be an independent predictor of long term outcome after CRT insertion in a study of 848 CRT recipients.[65] Following the landmark MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronisation Therapy) study, which demonstrated that CRT combined with implantable cardioverter defibrillator (ICD, CRT-D) decreased the risk of heart failure events in relatively asymptomatic patients with a low ejection fraction and wide QRS complexes,[66] a number of subsequent analyses have provided further interesting information. This includes data on the benefits of CRT in reducing the risk of recurring heart failure events[67] and atrial arrhythmias,[68] identifica- tion of additional factors that are associated with improved response to CRT[69 70] and with a super-response (defined by patients in the top quartile of LVEF change),[71] factors associated with greatest improvement in quality of life,[72] and information on optimal lead positioning of the LV lead.[73 74]

In a prospective, randomised controlled study to address whether ventricular dyssynchrony on echocardiography pre- dicted response to CRT, Diab et al found that the presence of echocardiographic dyssynchrony identified patients who derived the most improvement from CRT, although patients without dyssynchrony also showed more benefit and less deterioration with CRT than without. The authors concluded that the latter group of patients should not be denied CRT.[75]

CRT appeared to produce some benefits in patients with heart failure and a normal QRS duration, with patients experiencing an improve- ment in symptoms, exercise capacity and quality of life, although there was no difference in total or cardiovascular mor- tality in patients who received CRT compared with those receiv-ing optimal pharmacological management.[76] Among patients with heart failure and prolonged QRS duration who received a CRT device, those with a left bundle branch block (LBBB) morphology derived greater benefit (lower risk of ventricular arrhythmias and death and improved echocardiographic para- meters) compared with patients who had a non-LBBB QRS pattern (right bundle branch block (RBBB) or intraventricular conduction disturbances).[77]

The issue of whether CRT in patients undergoing atrioven- tricular (AV) junction ablation for permanent AF was superior to conventional RV pacing in reducing heart failure events was addressed in a prospective, randomised, multicentre study involving 186 patients.[78]

Over a median follow-up of 20 months (IQR 11–24 months) fewer patients in the CRT group (11%) experienced primary end point events (death from heart failure, hospitalisation due to heart failure or worsening heart failure) compared with patients in the RV group (26%; CRT vs RV group: sub-hazard ratio (SHR) 0.37, 95% CI 0.18 to 0.73; p=0.005).

Total mortality was similar in both groups. In a follow-up analysis looking at the predictors of clinical improvement after the 'ablate and pace' strategy, more patients in the CRT group responded to treatment (83% vs 63% in the RV group).[79] CRT mode and echo-optimised CRT were found to be the only independent protective factors against non- response (HR=0.24, 95% CI 0.10 to 0.58, p=0.001 and HR=0.22, 95% CI 0.07 to 0.77, p=0.018, respectively). In the PACE (Pacing to Avoid Cardiac Enlargement) trial, RV pacing in patients with bradycardia and preserved LVEF was associated with adverse LV remodelling and deterioration of systolic function at the second year, which was prevented by biventricular pacing.[80]

Heart block and pacemakers

The long term survival of older patients (average age 75 ±9 years) with Mobitz I second degree AV block was examined in a retrospective cohort study of 299 patients.[81] The investiga- tors found that 141 patients (47%) had a cardiac implantable electronic device (CIED) inserted during the follow-up period, of which 17 were ICDs. Patients with a CIED had greater cardiac comorbidity than those without a CIED, although CIED implantation was associated with a 46% reduction in mortality (HR 0.54, 95% CI 0.35 to 0.82; p=0.004). In another observational study of the impact of the ventricular pacing site on LV function in children with AV block, van Geldrop et al found that LV fractional shortening was significantly higher with LV pacing than with RV pacing.[82]

Further research on the topic of whether cardiac pacing is beneficial in patients with neurally mediated syncope suggests that dual chamber pacing may be useful in patients with severe asystolic forms. In the randomised multicentre ISSUE-3 trial (Third International Study on Syncope of Uncertain Aetiology) patients with syncope due to documented asystole on an implantable loop recorder were randomly assigned to dual chamber pacing with rate drop response or to sensing only.[83] Those assigned to dual chamber pacing had fewer syncopal epi- sodes during follow-up (32% absolute and 57% relative reduc- tion in syncope). A positive test with intravenous adenosine 5^0-triphosphate (ATP) has been shown to correlate with a subset of patients with neurally mediated syncope.[84]

A randomised, multicentre trial of the potential benefit of the ATP test in elderly patients (mean age 75.9±7.7 years) with syncope of unknown origin reported that active dual chamber pacing in those with a positive ATP test reduced syncope recurrence risk by 75% (95% CI 44% to 88%).[85] Long term outcome data on a distinct form of AV block, paroxysmal AV block, which cannot be explained by currently known mechanisms, suggest that these patients have a long history of recurrent syncope and may benefit from cardiac pacing, although in a small series of 18 patients (followed up for up to 14 years), no patient had per- manent AV block.[86]

The prognosis among healthy individuals admitted with their first episode of syncope was studied in a Danish nationwide registry involving 37 017 patients with syncope and 185 085 age and sex matched controls.[87] Patients who were admitted with syncope had significantly increased all cause mortality, cardiovascular hospitalisation, recurrent syncope and stroke event rates and were more likely to have a pacemaker or ICD inserted later.

CIED related infection

CIED infection is recognised as a significant cause of morbidity, mortality, and increased healthcare costs. The clinical character- istics, outcome, and health care implications of CIED related infections and endocarditis was analysed in a prospective cohort study using data from the International Collaboration on Endocarditis-Prospective Cohort Study (ICE-PCE) involving 61 centres in 28 countries.[88] CIED infection was diagnosed in 177 out of 2760 patients (6.4%). In-hospital and 1 year mortality rates were 14.7% (95% CI 9.8% to 20.8%) and 23.2% (95% CI 17.2% to 30.1%), respectively.

The rate of concomitant valve infection was high (found in 66 patients, 37.3%, 95% CI 30.2% to 44.9%) and early device removal was associated with improved survival at 1 year. In an attempt to assess the long term outcomes and predictors of mortality in patients treated according to current recommendations for CIED infection, Deharo et al conducted a two-group matched cohort study of 197 cases of CIED infection.[89] Long term mortality rates were similar between cases and matched controls (14.3% vs 11.0% at 1 year and 35.4% vs 27.0% at 5 years, respectively; both p=NS).

Independent predictors of long term mortality were older age, CRT, thrombocytopenia, and renal insufficiency. In another study examining whether the timing of the most recent CIED procedure influenced the clinical presentation and outcome of lead associated endocarditis (LAE), investigators found that early LAE presented with signs and symptoms of local pocket infection, whereas a remote source of bacteraemia was present in 38% of late LAE but only 8% of early LAE.[90] In-hospital mortality was low (early 7%; late 6%).

VENTRICULAR ARRHYTHMIAS AND SUDDEN CARDIAC DEATH

Epidemiology of sudden cardiac death

Sudden death is a frequent and well recognised risk in patients following myocardial infarction. In a study analysing data from 1067 patients from VALIANT (Valsartan in Acute Myocardial Infarction Trial) who had sudden death, investigators found that a high proportion of the deaths occurred at home, although in-hospital events were more common early on.[91] Patients who were asleep were more likely to have unwitnessed events. Although sudden cardiac death (SCD) and coronary artery disease (CAD) have many risk factors in common, certain clin- ical and electrocardiographic parameters may be useful to help separate out the two risks. For example, in a study of 18 497 participants from the ARIC (Atherosclerosis Risk in Communities) study and the Cardiovascular Health Study, Soliman et al found that after adjusting for common CAD risk factors, hypertension, increased heart rate, QTc prolongation, and abnormally inverted T waves were found to be stronger pre- dictors of high SCD risk.[92] In comparison, elevated ST segment height (measured at both the J point and 60 ms after the J point) was found to be more predictive of high incident CAD risk.

More research has also been performed on SCD in other sub- groups. In a prospective, national survey of sports related sudden death performed in France from 2005 to 2010, involv- ing subjects 10–75 years of age, investigators found that the overall burden of sudden death was 4.6 per million population per year, with 6% of cases occurring in young competitive ath- letes and more than 90% of cases occurring in the context of recreational sports.[93] Bystander cardiopulmonary resuscitation (CPR) and initial use of cardiac defibrillation were the strongest independent predictors for survival to hospital discharge, although bystander CPR was only initiated in one third of cases. In a retrospective autopsy study of 902 young adults (mean age 38±11 years) who had suffered non-traumatic sudden death, the cause of sudden death was attributed to a cardiac condition in 715 (79.3%) and unexplained in 187 (20.7%).[94] In another nationwide study on the incidence of SCD in persons aged 1–35 years, 7% of all deaths were attributed to SCD.[95] The incidence of SCD in the young, estimated to be 2.8% per 100 000 person-years, was higher than previously reported. Risk factors for SCD in post-menopausal women may include more novel parameters, such as higher pulse, higher waist-to-hip ratio, ele- vated white blood cell count, and ethnicity (African Americans having a higher risk) as well as traditional risk factors.[96]

More intense research has been conducted in a variety of set- tings on the early repolarisation syndrome (ERS) since landmark studies showed a link with idiopathic ventricular fibrillation and sudden death.[97] [98] These include studies on ERS on cardiac arrest survivors with preserved ejection fraction,[99] in families with sudden arrhythmic death syndrome[100] and other families with an early repolarisation pattern on the ECG,[101] and in Asian populations.[102] However, there is still some controversy over the exact clinical significance of these ECG findings and what the implications are.[103] [104]

The genetics of inherited cardiac conditions and how specific genotypes can lead to clinical manifestations of disease, affect SCD risk or guide management continues to attract intense interest.[105-108] Results from the DARE (Drug-induced Arrhythmia Risk Evaluation) study, in which 167 single nucleo- tide polymorphisms spanning the NOS1AP gene, were evaluated in 58 Caucasian patients who had experienced drug induced QT prolongation and 87 Caucasian controls, demonstrated that common variations in the NOS1AP gene were associated with a significant increase in drug induced long QT syndrome.[109] This may have clinical implications for future pharmacogenomics testing in patients at risk of drug induced long QT syndrome and safer prescribing.

In another study assessing whether non- cardiovascular hERG (human Ether à go-go-Related Gene) channel blockers are associated with an increased risk of SCD in the general population, investigators compared 1424 cases of SCD with 14 443 controls.[110]

Use of hERG channel blockers was found to be associated with an increased risk of SCD and drugs with a high hERG channel inhibiting capacity had a higher risk of SCD than those with a low hERG channel inhibit- ing capacity.

Implantable cardioverter defibrillators

The clinical parameters associated with death before appropriate ICD therapy in patients with ischaemic heart disease who had an ICD inserted for primary prevention were assessed in a retro- spective cohort study of 900 patients.[111] The investigators found that New York Heart Association (NYHA) functional class ≥ III, advanced age, diabetes mellitus, LVEF ≤25%, and a history of smoking were significant independent predictors of death without appropriate ICD therapy, and suggested that this information may facilitate a more patient tailored risk estima- tion. Another risk score for predicting acute procedural compli- cations or death after ICD implantation using 10 readily available variables from 268 701 ICD implants was developed to provide useful

information in guiding physicians on patient selection and determining the intensity of post-implant care required.[112] A risk score aimed at predicting the long term (8 years) benefit of primary prevention ICD implantation was applied to 11 981 patients from the MADIT-II trial.[113] The investigators found that patients with low and intermediate risk (0 or 1–2 risk factors, respectively) benefitted more from ICD implantation, compared with patients with high risk (≥3 risk factors) who had multiple comorbidities, in which there was no significant difference in 8 years survival between ICD and non-ICD recipients.

Another risk score for the prediction of mortality in Medicare beneficiaries receiving ICD implantation for primary prevention was developed from a cohort of 17 991 patients and validated in a cohort of 27 893 patients.[114] Over a median follow-up of 4 years, 6741 (37.5%) patients in the development cohort and 8595 (30.8%) patients in the validation cohort died. Seven clinically relevant predictors of mortality were identified and used to develop a model for determining those patients at highest risk for death after ICD implantation. Future selection of ICD recipients for primary prevention ICDs may therefore be refined and more personalised to the individual patient's risk/ benefit profile with the use of such models, rather than being based predominantly on LVEF, as is recommended by current guidelines.

Other investigations, such as cardiac magnetic resonance (CMR) imaging to identify and characterise myocardial scar, may be a useful addition to future risk stratification of patients for primary prevention ICD implantation. The ability of scar characteristics assessed on CMR to predict ventricular arrhyth- mias was evaluated in a study of 55 patients with ischaemic car- diomyopathy who received an ICD for primary prevention and in whom CMR with late gadolinium enhancement had been performed before ICD implantation.[115] All CMR derived scar tissue characteristics were found to be predictive for the occur- rence of ventricular arrhythmias, supporting the potential use of this imaging modality to help refine risk stratification of patients and improve selection for ICD implantation. This finding was further supported by a prospective study of 137 patients evalu- ated with CMR before ICD implantation for primary preven- tion.[116] Myocardial scarring on CMR was found to be an independent predictor of adverse outcomes. Patients with sig- nificant scarring (>5% of the left ventricle) with LVEF >30% had a similar risk to those with LVEF ≤30%, while in patients with LVEF ≤30%, minimal or no scarring was associated with low risk, similar to those with LVEF >30%.

The use of intracardiac ICD parameters to assess risk has also received further attention. In a prospective, multicentre study of 63 ICD patients, T wave alternans and non-alternans variability (TWA/V) was found to be significantly greater before ventricular tachycardia/ventricular fibrillation (VT/VF) episodes than during baseline rhythm.[117] The investigators suggested that continuous measurements of TWA/V from the intracardiac ICD electro- grams may be a useful parameter to detect impending VT/VF and allow the device to initiate pacing therapies to prevent the ventricular arrhythmias from occurring. In contrast, an early analysis of a prospective, single centre study on the use of ICD based ischaemia monitoring on clinical care and patient manage- ment reported that this parameter was not clinically useful and actually increased the number of unscheduled outpatient visits in patients with this feature on their ICD compared with patients with ICDs without this capability.[118]

Reports on the complications and negative aspects of ICDs include problems associated with the Sprint Fidelis ICD leads[119-121] and potential psychological impact and phobic anxiety among ICD recipients.[122] In a study of 3253 patients from 117 Italian centres who underwent de novo implantation of a CRT-D device, investigators found that device related events were more frequent in patients who received CRT-D devices compared with those who received ICDs only (single or dual chamber), although these events were not associated with a worse clinical outcome.[123] In a multicentre, longitudinal cohort study of 104 049 patients receiving single and dual chamber ICDs, dual chamber device implantation was more common, but was associated with increased peri-procedural complications and in-hospital mortality compared with single chamber ICDs.[124] A retrospective, single centre cohort study of 334 hypertrophic cardiomyopathy patients with ICDs reported that this group of patients had significant cardiovascular mortality and were exposed to frequent inappropriate shocks and implant complications.[125] Adverse ICD related events (inappropriate shocks and/or implant complications) were seen in 101 patients (30%; 8.6% per year), and patients with CRT-D were more likely to develop implant complications than those with single chamber ICDs and had a higher 5-year cardiovascular mortality rate.

Strategies to reduce ICD complications and inappropriate shocks include using special diagnostic ICD algorithms to iden- tify potential lead problems early,[126] and changes in ICD pro- gramming with a prolonged delay in therapy for tachyarrhythmias of ≥200 beats/min or higher, as demonstrated in the MADIT-RIT (MADIT-Reduction in

Inappropriate Therapy) trial.[127] Increasing clinical experience is also being gained in the use of subcutaneous ICDs,[128 129] which holds great potential in reducing some types of ICD related complica- tions, although an initial learning curve needs to be overcome first. Real world data of ICD implantation and use show that patients treated by very low volume operators (physicians who implanted ≤1 ICDs per year) were more likely to die or experi- ence cardiac complications compared with operators who fre- quently performed ICD implantation.[130] Another strategy to reduce ICD complications is to improve the selection process of those patients who would truly benefit from these devices. In an observational outcome study of consecutive subjects referred to a regional inherited cardiac conditions clinic because of a rela- tive who had sudden unexpected death, the number of ICDs inserted as a result of specialist assessment was found to be very small (2%).[131]

Out-of-hospital cardiac arrest

Survival from out-of-hospital cardiac arrest (OHCA) appears to have increased over the past several years, probably as a result of better pre-hospital care (early recognition, more effective CPR, faster emergency services response) and advances in the hospital management of patients following OHCA.[132 133] Data from the London Ambulance Service's cardiac arrest registry from 2007 to 2012 showed an improvement in OHCA survival over the 5 year study period.[134] In an observational Swedish registry study of 7187 patients with OHCA over an 18 year period, bystander CPR was found to increase from 46% to 73% (95% CI for OR 1.060 to 10.081 per year), early survival increase from 28% to 45% (95% CI 1.044 to 1.065), and survival to 1 month increase from 12% to 23% (95% CI 1.058 to 1.086).[135] Strong predictors of early and late survival were a short interval from collapse to defibrillation, bystander CPR, female gender, and place of collapse. A large prospective cohort study of OHCA in North American adults involving 12 930 subjects (2042 occurring in a public place and 9564 at home) also found that the rate of survival to hospital discharge was better for arrests in public settings with automated external defi- brillators (AEDs) applied by bystanders compared to those that occurred at home (34% vs 12%, respectively; adjusted OR 2.49, 95% CI 1.03 to 5.99; p=0.04).[136] Hospital characteristics asso- ciated with improved patient outcomes following OHCA were analysed from the Victorian Ambulance Cardiac Arrest Registry of 9971 patients over an 8 year period.[137] Outcome following OHCA was found to be significantly improved in hospitals with 24 h cardiac interventional services (OR 1.40, 95% CI 1.12 to 1.74; p=0.003) and patient reception between 08.00 and 17.00 h (OR 1.34, 95% CI 1.10 to 1.64; p=0.004). OHCA in children was assessed in a prospective, population based study of victims younger than 21 years of age.[138] The incidence of paediatric OHCA was 9.0 per 100 000 paediatric person-years (95% CI 7.8 to 10.3), whereas the incidence of paediatric OHCA from cardiac causes was 3.2 (95% CI 2.5 to 3.9). The authors concluded that OHCA accounts for a significant propor- tion of paediatric mortality, although the vast majority of OHCA survivors have a neurologically intact outcome.

Studies on the optimal sequence of CPR measures to use in OHCA patients have reported varying results. In a meta-analysis of four randomised controlled clinical trials enrolling 1503 sub- jects with OHCA, no significant difference was found between chest compression first versus defibrillation first in the rate of return of spontaneous circulation, survival to hospital discharge or favourable neurologic outcomes, although subgroup analyses suggested that chest compression first may be beneficial for cardiac arrests with a prolonged response time.[139] In a more recent, nationwide, population based observational study involv- ing OHCA patients in Japan who had a witnessed arrest and received shocks with public access AED, compression only CPR was found to be associated with a significantly higher rate of survival at 1 month and more favourable neurological outcomes compared with conventional CPR measures (chest compression and rescue breathing).[140] However, for children and younger people who have OHCA from non-cardiac causes, and in people in whom there was a delay in starting CPR, other studies have suggested that conventional CPR is associated with better outcomes than chest compression only CPR.[141 142]

CONCLUSIONS

Important progress has been made over the past few years in our understanding of basic and clinical cardiac electrophysiology which have advanced and improved the management of patients with heart rhythm disorders. Multiple studies have demon- strated an association between AF and various systemic condi- tions and novel risk factors. These studies highlight the importance and complexity of this complex arrhythmia and further support the notion that AF is a systemic condition. Although many of these associations have not been shown to play a causal role, they may nonetheless prove useful clinically in future risk stratification scores for the diagnosis or treatment of AF. More research is still

needed to increase our understand- ing of the underlying mechanisms responsible for the develop- ment and progression of AF and which patient subgroups will benefit most from specific treatments or the different options for anticoagulation.

The field of CRT and pacing has also progressed rapidly over the past few years with a lot of interest in the optimal clinical parameters for selection of patients, prediction of response, and adverse remodelling. Similarly, as our understanding of the sub- strate responsible for ventricular arrhythmias and SCD improves, the selection of suitable candidates for ICD therapy is becoming more refined. Research into the complications asso- ciated with implantable cardiac devices, such as device infection and inappropriate shocks from ICDs, remains important as indi- cations for device implantation continue to expand and more and more patients with existing devices undergo device replace- ment procedures.

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Caractéristiques et pronostic hospitalier de l'endocardite infectieuse : Données d'une expérience monocentrique de 15 ans

Characteristics and in hopital outcomes of infective endocarditis : single-center experience of 15 years

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Résumé

Introduction. Malgré une amélioration constante des modalités de prise en charge de l'endocardite infectieuse (EI), celle-ci reste associée à une morbi-mortalité élevée.
But de l'étude. Dans ce travail, nous nous proposons d'étudier les caractéristiques anatomo-cliniques de l'EI ainsi que son pronostic hospitalier.
Population et méthodes. Nous avons étudié rétrospectivement les données cliniques, biologiques et d'imagerie ainsi que le pronostic de 234 patients admis dans notre service entre janvier 1997 et décembre 2011 pour EI. Le diagnostic a été établi conformément aux critères de la Duke University.
Résultats. L'âge moyen de la population de l'étude était de 36.5 ±17 ans avec 56% de sujets de sexe masculin. Un antécédent de rhumatisme articulaire aigu a été relevé dans 50% des cas. Il s'agissait d'une EI sur prothèse valvulaire dans 25.2% des cas. Aucune porte d'entrée n'a pu être identifiée dans 49.7% des cas et le Staphylococcus aureus a été isolé dans 23.9% des cas. Une ou plusieurs végétations ont été identifiées à l'échocardiographie dans 81.6% des cas avec 41.8% de localisation mitrale. La mortalité hospitalière était de 18.4%. Les facteurs qui y sont associés en analyse univariée étaient l'insuffisance cardiaque, l'embolie périphérique, l'accident vasculaire cérébral (AVC) hémorragique et l'abcès cérébral. En analyse multivariée, seuls l'insuffisance cardiaque, l'embolie périphérique et les AVC hémorragiques étaient indépendamment associés au décès intra-hospitalier.
Conclusion. La mortalité hospitalière de l'EI reste élevée y compris au cours des dernières années. L'insuffisance cardiaque et les AVC restent des facteurs prédictifs majeurs du décès intra-hospitalier.

Mots-clés
Endocardite
Valvulopathie
Mortalité

Summary

Background. Despite steady improvements in management strategies, morbidity and mortality in infective endocarditis (IE) remain high.
Aim of the study. We sought to study anatomical and clinical features and in-hospital prognosis of IE.
Methods. In this retrospective study, we collected clinical, biological and imaging data about 234 patients who presented to our department between January 1997 and December 2011 with the diagnosis of IE. Duke criteria were applied for IE diagnosis.
Results. Mean age of the study population was 36.5 ±17 years and prevalence of male gender was 56%. History of rheumatic fever was reported in 50% of patients. IE involved a prosthetic valve in 25.2% of patients. No access site could be identified in 49.7% of cases and Staphylococcus aureus could be isolated in 23.9% of cases. One or more vegetations could be identified on echocardiography in 81.6% of cases and mitral valve was involved in 41.8% of cases. In-hospital mortality was at 18.4%. In univariate analysis, factors associated with in-hospital death were heart failure, peripheral embolism, hemorrhagic stroke and cerebral abscess. In multivariate analysis, factors independently associated with in-hospital death were heart failure, peripheral embolism and hemorrhagic stroke.
Conclusion. In this study, in-hospital mortality in IE remains high even lately. Heart failure and stroke remain the major predictive factors of in-hospital death.

Keywords
Endocarditis
Valvulopathy
Mortality

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INTRODUCTION

Malgré des avancées importantes dans la prise en charge médico-chirurgicale au cours des dernières années, l'endocardite infectieuse (EI) continue à être à l'origine d'une morbi-mortalité élevée. Celle-ci reste particulièrement préoccupante dans les pays en voie de développement. [1] A l'origine de ce pronostic fâcheux on accuse une présentation clinique déroutante, un diagnostic souvent fait tardivement et une résistance sans cesse grandissante des germes incriminés aux agents antimicrobiens. Le diagnostic précoce, un traitement antimicrobien approprié, une évaluation précise des lésions cardiaques et extra-cardiaques et une intervention chirurgicale indiquée à temps restent les seuls garants d'un meilleur pronostic. Dans cette étude, nous reprenons le profil épidémiologique et évolutif ainsi que le pronostic et les facteurs prédictifs de mortalité de l'EI à travers une expérience Tunisienne monocentrique de 15 ans.

POPULATION ET MÉTHODES

Il s'agit d'une étude menée dans le service de cardiologie de l'hôpital universitaire Fattouma Bourguiba de Monastir, Tunisie, portant sur des patients hospitalisés consécutivement entre Janvier 1997 et Décembre 2011, le diagnostic d'EI étant établi selon les critères de la *Duke University* [2]. La collecte des données s'est basée sur les informations disponibles sur les dossiers médicaux. Nous avons relevé les caractéristiques épidémiologiques, les données cliniques, biologiques et le pronostic hospitalier de ces patients. L'insuffisance cardiaque a été définie par un tableau clinique associant dyspnée, tachycardie, des râles crépitants et des images radiologiques de congestion pulmonaire. Un état de choc (EDC) a été défini par une pression artérielle systolique (PAS) inférieure à 90 mm Hg associée à une défaillance rénale. Un accident vasculaire cérébral (AVC) a été défini par la survenue brutale d'un déficit neurologique systématisé en rapport avec une embolie artérielle ou une hémorragie cérébrale. La récidive précoce a été définie comme étant la survenue d'une endocardite dans l'année qui suit une endocardite antérieure guérie.
Les données biologiques comportaient la numération de la formule sanguine (NFS), les hémocultures (HC) avec cultures en milieux aérobie et anaérobie, la créatininémie et la clairance de la créatinine. L'insuffisance rénale a été définie par un taux de créatinine supérieur à 120 µmol/L. L'échocardiographie Doppler trans-thoracique (ETT) ou trans-oesophagienne (ETO), permettait à la fois une confirmation du diagnostic et une localisation de l'EI. Les végétations sont definies comme étant des masses denses, appendues à une structure valvulaire. Les abcès ont été définis comme étant des zones périvalvulaires vides d'échos [3].
Le traitement était médico-chirurgical. Les indications de la chirurgie étaient une dysfonction valvulaire sévère avec retentissement hémodynamique, abcès valvulaire ou péri-valvulaire, les végétations volumineuses avec risque important d'enclavement ou d'embolie et l'échec de l'antibiothérapie.
Les complications étudiées ont été l'embolie systémique, l'AVC, l'embolie pulmonaire, l'insuffisance cardiaque, l'EDC, l'abcès intracardiaque. Les éléments de surveillance à moyen et à long termes ont été la récidive d'endocardite, le recours à une chirurgie ultérieure et le décès.
Analyse statistique. Les variables quantitatives sont exprimées en moyennes ±DS et les variables qualitatives présentées en valeur absolue et pourcentage.
Le test du X^2 a été utilisé pour déterminer les facteurs prédictifs de mortalité hospitalière en analyse univariée. L'analyse multivariée des facteurs retenus a été faite par regression logistique binaire. Le seuil de significativité a été fixé à 0.05. L'analyse statistique a été réalisée par le Logiciel SPSS 17.0.

RÉSULTATS

Nous avons colligé 234 cas d'EI durant la période d'étude. L'âge moyen de nos patients était de 36,5±17,7 années et la prévalence du sexe masculin était de 131 (56%). Les antécédents pathologiques des patients sont représentés dans le tableau 1.

Tableau 1. Principaux antécédents retrouvés dans la population d'étude.

Antécédents	Fréquence, %
Cardiopathies rhumatismales	117 (50%)
Diabète	24 (10,3%)
Cardiopathie congénitale	20 (8,5%)
Endocardite infectieuse	13 (5,6%)
Pacemaker	7 (3%)

Une cardiopathie rhumatismale sous-jacente était notée dans 117 (50%) cas. L'EI intéressait une prothèse valvulaire ou plus dans 59 (25,2%) cas. A l'admission, une dyspnée stade III ou IV de la New York Heart Association (NYHA) était retrouvée chez 82 (35%) patients, une insuffisance ventriculaire droite était notée dans 65 (27,8%) cas. Dix-neuf patients (8,1%) ont été admis en état de choc. La porte d'entrée (tableau 2) était bucco-dentaire dans 65 cas (27,8%). Le taux d'hémoglobine moyen était de 10,2±2,5g/dl, le bilan inflammatoire a montré un taux de C-réactive protéine (CRP) moyen à 102,4±54 mg/l. Le taux moyen de créatinine plasmatique à l'entrée était à 123,6±108µmol/l. Les hémocultures étaient positives chez 109 (46,6%) patients. Les germes

isolés sont représentés sur le tableau 3. Aucun germe n'a été isolé chez 127 (54,2%) patients.

Tableau 2. Portes d'entrées d'endocardite dans la population d'étude.

Porte d'entrée	Fréquence n,%
Bucco dentaire	65 (27,9 %)
Pulmonaire	19 (8,1 %)
Cutanée	17 (7,3 %)
Urinaire	11 (4,7 %)
Veineuse	6 (2.6%)
Indéterminée	116 (49.7 %)

Tableau 3. Germes isolés dans la population d'endocardites infectieuses.

Germe	Fréquence n,%
Aucun germe isolé	127 (54.2%)
Staphylocoque	56 (23.9%)
Streptocoque	24 (10.3%)
Entérobactéries	8 (3.4%)
Autres	19 (8.1%)

L'ETT a mis en évidence une ou plusieurs végétations chez 191 (81,6%) patients ; elles intéressaient le cœur droit chez 15 (6,4%) patients. Un abcès intra-cardiaque a pu être visualisé dans 23 (9,8%) cas. Une rupture de cordages a été mise en évidence dans 8 cas (3,4%). L'ETO a été réalisée chez 210 (89,7%) patients. Le tableau 4 reprend les caractéristiques échocardiographiques des patients.

Tableau 4. Caractéristiques échographiques des endocardites infectieuses.

Végétation identifiée à l'ETT	**191(81.6%)**
Végétation mitrale	**98 (41.8%)**
Végétation aortique	**66 (28.2%)**
Végétation mitro-aortique	**7 (3%)**
Végétation tricuspide	**15 (6.4%)**
Sonde de stimulation/Pacemaker	**5 (2.2%)**
Végétation >10 mm	**130 (55.5%)**
Végétation >15 mm	**22 (9.4%)**
Abcès de l'anneau	**13 (5.6%)**
Rupture de cordage	**8 (3.4%)**

ETT : échocardiographie transthoracique

Selon les critères de la *Duke University*, l'EI était certaine dans 177 (75,6%) cas et probable dans 57 (24,4%) des cas.
Les complications sont rapportées dans le tableau 5. Une insuffisance cardiaque gauche a été noté chez 72 (30,8%) patients. Un accident embolique a été rapporté dans 76 (32,4%) cas dont 37 (15,8%) AVC ischémiques. On a rapporté 14 (6%) cas d'hémorragie cérébrale.
Une chirurgie a été réalisée chez 115 (49.4%) patients, l'indication chirurgicale étant posée sur des arguments hémodynamiques dans 87 (75.7%) cas et des arguments septiques dans 22(19.1%) cas.

Tableau 5. Complications de l'endocardite infectieuse

Complication	Fréquence n,%
Insuffisance cardiaque	72 (30,8%)
Accident embolique	39 (16,7%)
AVC ischémique	37 (15,8%)
Hémorragie cérébrale	14 (6%)
Anévrysme mycotique	14 (6%)

AVC : accident vasculaire cérébral

La mortalité hospitalière était de 43 (18.4%) cas. Les rechutes et les récidives étaient retrouvées respectivement chez 12 (5,1%) et 10 (4,3%) patients. La guérison totale a pu être notée dans 183 (78,2%) cas.
En analyse univariée, la mortalité hospitalière était significativement associée
à l'insuffisance cardiaque (53.5% vs. 25.9%, p=0.01), à une embolie périphérique (32.6% vs. 15.9%, p=0.017), à l'AVC hémorragiques (16.3 vs. 3.7%, p=0.006), à l'abcès cérébral (7% vs. 0.5 %, p=0.021) (tableau 6). Par ailleurs, le taux de créatinine plasmatique était significativement plus élevé chez les patients décédés (153.5 µmol/l vs. 117.3µmol/l, p=0.03).
Aucune corrélation n'a été notée en ce qui concerne les AVC ischémiques (23.3% vs. 14.3 %, p=0.167). En analyse multivariée, les éléments prédictifs de mortalité intra-hospitalière sont l'insuffisance cardiaque (OR =3.8, 95% CI : 1.8-7.9, p<0.001), les accidents emboliques (OR=2.29, 95% CI : 1.01-5.2, p=0.047), les accidents vasculaires cérébraux hémorragiques (OR =6.06, 95% CI : 1.8-19.5, p=0.003).
Le suivi long terme a concerné 61 (26.2%) patients avec un suivi moyen de 3.43 ±5 ans et des extrêmes allant de 0.12 à 20 années. Une récidive d'EI a été notée dans 34 (14.52%) cas. Trente-deux (94.11%) patients ont bénéficié d'une chirurgie et 2 (5.89%) patients étaient décédés.

Tableau 6. Facteurs prédictifs de mortalité intra-hospitalière en analyse univariée dans l'endocardite infectieuse.

	Survivants (n=190)	Décédés (n=43)	P
Embolies périphériques	30 (15.78%)	14 (32.55%)	0.01
Abcès cérébral	1 (0.5 %)	3 (7%)	0.02
Insuffisance cardiaque	49 (25.78%)	23 (53.5%)	0.01
Etat de choc	13 (6.84%)	6 (14%)	0.28
Insuffisance rénale	148 (77.89%)	33 (76.74%)	0.83
AVC hémorragique	7 (3.7%)	7 (16.27%)	0.006
AVC ischémique	27 (14.21%)	10 (23.25%)	0.16

DISCUSSION

L'incidence de l'EI est restée relativement stable depuis une trentaine d'années [4]. Elle touche préférentiellement l'homme, avec une prévalence entre 60 et 70% et un âge moyen de 50 à 55 ans [5,6]. Dans les séries africaines on trouve que cette maladie touche préférentiellement la population jeune du fait de la prédominance des valvulopathies rhumatismales [7-9]. Les résultats de notre série n'échappent pas à cette règle.

La recherche d'une porte d'entrée est fréquemment négative, cependant l'origine bucco-dentaire reste le plus souvent incriminée [10].

D'après la littérature, Les trois germes les plus fréquemment isolés sont le streptocoque, le staphylocoque et les entérobactéries. Les staphylocoques (S. Aureus et à Coagulase négative) représentent plus de 30 % des causes bactériennes d'EI [11]. Dans notre série, le staphylocoque a été incriminé dans 23.9% des cas.

Le taux d'EI à HC négative reste élevé (54.2%). Dans la littérature, ce taux est assez fluctuant [10] en fonction des différences de performance technique et des méthodes de diagnostic microbiologique. Les deux justifications les plus fréquemment avancés pour expliquer la négativité des HC sont l'administration préalable d'antibiotiques et les germes à culture fastidieuse ou lente [12].

L'échocardiographie Doppler joue un rôle important dans le diagnostic de l'EI et reste l'examen de première intention en cas de suspicion diagnostique. Bien que l'ETO soit plus sensible que l'ETT [7], dans notre série, cette dernière a permis d'objectiver des végétations chez la majorité de nos patients (81,6%). L'ETO a été réalisé en cas de non confirmation du diagnostic par ETT pour une meilleure appréciation des lésions valvulaires ou en cas d'EI sur prothèse.

L'insuffisance cardiaque reste la complication cardiaque la plus fréquente de l'EI et la première cause de mortalité. Elle est observée chez 60 à 70 % des malades atteints d'EI hospitalisés en centre spécialisés [13-15].

Les complications neurologiques sont moins fréquentes mais restent préoccupantes, elles peuvent être une circonstance de découverte dans 29% des cas [16,17]. Dix à 40 % des patients atteints d'une EI présentent un événement neurologique au cours de leur évolution dont 60 % d'AVC ischémiques.

Les accidents emboliques résultent d'une fragmentation de la végétation, et conduisent selon leur taille, à l'obstruction de vaisseaux de plus ou moins gros calibre. Les embolies atteignent les viscères abdominaux (rate, reins, structure digestive), plus rarement le squelette et les extrémités dans 50% des cas. Les épisodes d'embolies sont particulièrement fréquents lors d'endocardite à Staphylococcus aureus ou à champignons [18].

L'EI est une pathologie grevée d'un taux de mortalité hospitalière élevée. Ce taux s'élève à 18.2% dans notre série et reste globalement supérieur à ceux rapportés dans la littérature (9.6 à 26%) [19-22]. En analyse multivariée les facteurs prédictifs de mortalité intra-hospitalière sont l'insuffisance cardiaque (OR = 3.8), les accidents emboliques (OR = 2.28) et les AVC hémorragiques (OR =6.06). Dans la littérature, l'insuffisance cardiaque est le plus important facteur prédictif de mortalité hospitalière et à moyen terme [20,23]. Les AVC et l'insuffisance rénale sont des complications ayant un important impact sur le taux de mortalité hospitalière et à moyen terme [24].

CONCLUSION

Malgré les avancées techniques en échocardiographie et en diagnostic microbiologique, l'instauration d'une antibiothérapie adaptée et le recours de plus en plus précoce à la chirurgie, le pronostic de l'EI en milieu de cardiologie demeure toujours aussi préoccupant durant les 15 dernières années. La mortalité hospitalière dans notre centre n'a pas diminué en comparaison aux données des grandes séries des années 90. Un diagnostic précoce et des investigations poussées même pour un faible degré de suspicion seraient les garants d'un meilleur pronostic ultérieurement.

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Almanac 2013—stable coronary artery disease

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CORONARY HEART DISEASE IN DECLINE

Epidemiological data from Europe, the USA and elsewhere in the developed world show a steep decline in coronary heart disease (CHD) mortality during the last 40 years.[1] Concern about levelling of mortality rates in younger adults[2] has been somewhat alleviated by data from The Netherlands showing that in men aged <55 years, rates of decline have again accelerated, increasing from only 16% in 1993–1999 to 46% in 1999–2007.[3] A similar pattern was observed in young women with rates of decline of 5% and 38% during the same time periods. This is encouraging, particularly in the context of data from Denmark and the UK showing declining mortality and also a sharp fall in standardised incidence rates for acute myocardial infarction indicating that coronary prevention, as well as acute treatments, has contributed to recent mortality trends.[4] [5] Meanwhile an Australian study reminds us that myocardial infarction is but one of several manifestations of cardiovascular disease by reporting that decreasing incidence and recurrence rates for hospitalised CHD from 2000 to 2007 have also been seen for cerebrovascular and peripheral arterial disease.[6]

However, the epidemiological news is not all good, and data from the UK show that the pernicious relationship between socioeconomic status (SES) and CHD has shown no tendency to go away in recent years, the gradients between top and bottom SES quintile groups for hospital admissions remaining essentially unchanged across the age range.[7] Whether this has contributed to the almost 3-fold risk of myocardial infarction associated with stillbirth and 9-fold risk associated with recurrent miscarriage in a recent German study is unclear because the investigators made no adjustment for SES.[8] Nor is it clear if SES has contributed to the persistent ethnic differences in both US and UK studies of CHD mortality although other factors appear also to be important. Thus, African-American men have greater exposure to CHD risk factors than Caucasians and, when adjustment is made for this, their susceptibility to CHD is no greater, although mortality rates are twice as high.[9] For African-American women, incidence and mortality rates are higher than their Caucasian counterparts. These findings suggesting that exposure to risk factors contributes to ethnic differences in the incidence of CHD are to some extent reflected in a recent report from the Health Survey for England in which 13 293 Caucasian and 2120 S Asians consented to mortality follow-up.[10] Physical inactivity increased susceptibility to disease and not by increased case-fatality rates.[11]

DIAGNOSIS OF STABLE CORONARY ARTERY DISEASE

The recent AHA/ACC guideline update[12] emphasised the importance of individualising the diagnostic workup based on the estimated probability of coronary artery disease. In this respect, it mirrored an earlier National Institute of Clinical Excellence (NICE) guideline on chest pain diagnosis,[13] but there were important differences in the recommendations for non-invasive testing, the new AHA/ ACC guideline preferring the exercise ECG as the initial diagnostic approach for most patients, (NICE had previously counselled against use of the exercise ECG based on its relatively poor diagnostic performance) with pharmacologic radionuclide, cardiac MRI or stress

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echocardiography testing in reserve for patients unable to exercise. Recommendations for cardiac CT coronary angiography (CTCA) were cautious, and invasive angiography was recommended for diagnostic purposes only if the results of non-invasive testing suggested a high likelihood of severe 3-vessel or left main coronary artery disease, and the patient was willing to undergo revascularisation. In general, therefore, the AHA/ACC guideline update was less prescriptive than the earlier NICE guideline, perhaps partly because it put less emphasis on the cost effectiveness of its recommendations.

MANAGEMENT OF STABLE CORONARY ARTERY DISEASE

The recent NICE guideline[14] recommended initial treatment with a short-acting nitrate and a ¤blocker and/or a calcium channel blocker for control of angina plus aspirin and a statin for secondary prevention. Lifestyle measures were also emphasised. For patients with continuing symptoms cardiac catheterisation with a view to revascularisation was recommended, additional antianginal treatment (long-acting nitrates or one of the newer agents) only being indicated for patients unsuitable for revascularisation.

It was further recommended that the mode of revascularisation (percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG)) should best be determined by a multidisciplinary group, a recommendation that has also been emphasised by European guideline groups,[15] bearing in mind the potential for prognostic benefit from CABG in patients with complex multivessel and left main stem disease,[16] Caucasians (47% vs 28%) and explained >20% of their excess CHD mortality. Certainly, the emerging consensus is that the excess CHD mortality among UK S Asians is driven almost entirely by theirsymptoms adequately controlled with medical treatment, the guideline recommended discussion of the potential for prognostic improvement with CABG. Those patients prepared to proceed to CABG might then be offered diagnostic cardiac catheterisation to rule out complex multivessel and left main stem disease, which a recent meta-analysis reported in as many as 36% (18.5–48.8%) of cases of stable coronary disease selected for cardiac catheterisation.[17]

SECONDARY PREVENTION OF STABLE CORONARY DISEASE

The scope for improving secondary prevention in patients with stable coronary artery disease has been emphasised in two recent reports. In The multinational REduction of Atherothrombosis for Continued Health (REACH) Registry, 20 588 symptomatic patients were analysed for 'good control' of cardiovascular risk factors, defined as three to five of systolic blood pressure <140 mm Hg, diastolic blood pressure <90 mm Hg, fasting glycaemia <110 mg/dL, total cholesterol <200 mg/dL, non-smoking.[18] Only 59.4% had good control of risk factors at baseline, but this was associated with lower mortality (OR 0.89; 95% CI 0.79 to 0.99) at 36 months, compared with poor control. In the UK ASPIRE-2-PREVENT survey, 676 patients with CHD (25.6% women) had the following rates of major risk factors: smoking 14.1%, obesity 38%, physical inactivity 83.3%, blood pressure ≥130/80 mmHg, total cholesterol ≥4 mmol/L and diabetes 17.8%, leading the authors to conclude that there is considerable potential for reducing cardiovascular risk in these patients and thereby improve prognosis.[19] Clopidogrel. The availability of low-cost generic clopidogrel prompted a NICE review of its cost effectiveness which recommended it should now supersede aspirin in certain high-risk groups, namely patients with multivascular disease, peripheral vascular disease and myocardial infarction.[20] However, clopidogrel is metabolised by enzymes in the hepatic cytochrome P450 (CYP) system, and variability in its antiplatelet activity may occur because the activity of these enzymes is influenced by common genetic variations, and also by a number of commonly used drugs. Several studies have reported loss-of-function alleles in CYP2C19 that result in reduced activation of clopidogrel[21] and a modest lowering of antiplatelet activity[22] which have been associated with an increased risk of cardiovascular events in some meta-analyses.[23] Conversely, gain-of-function alleles have been associated with reduced cardiovascular risk among clopidogrel-treated patients[24] A recent meta-analysis, however, has commented on the tendency of small studies to bias conclusions about the way genetic variants influence clinical outcomes, and in larger studies of clopidogrel therapy with ≥200 outcome events found no effect of loss-of-function alleles on cardiovascular risk.[25] At present, therefore, there seems to be no compelling

indication for genetic testing to guide clopidogrel treatment although the topic remains a subject of ongoing debate. Also debated is the interaction of clopidogrel with some commonly used drugs, particularly proton pump inhibitors (PPI) and amlodipine. A recent meta-analysis of studies of PPIs in patients treated with clopidogrel found clear evidence of reduced platelet activity but although clinical outcomes appeared adversely affected by the interaction, the authors urged cautious interpretation, pointing out the heterogeneity caused by retrospective studies. When analysis was restricted to prospective studies of PPIs and clopidogrel, adverse clinical consequences could no longer be demonstrated (OR 1.13 (0.98 to 1.30)).[26] Similarly, the clinical impact of amlodipine on responsiveness to clopidogrel remains uncertain. Certainly, there is evidence of interaction, and in one study of 1258 patients receiving clopidogrel, amlodipine administration was associated with higher on-treatment platelet reactivity only in those patients with a loss-of-function P450 (CYP) genotype (249±83 vs 228±84 P2Y12 reaction units), and this was associated with a higher incidence of cardiovascular events (4.6% vs 0.6%).[27] However, in a more recent randomised trial, platelet function in 98 patients with stable coronary artery disease taking clopidogrel was similar regardless of amlodipine therapy.[28] At present, therefore, there is no guideline recommendation about concomitant prescription of these drugs in patients taking clopidogrel.

Statins, Niacin and cholesteryl ester transfer protein (CETP) inhibitors. The benefits of statins for secondary prevention in patients with stable coronary artery disease are well established. Cardiovascular endpoints are reduced in proportion to the degree of LDL-cholesterol reduction, probably in response to stabilisation and regression of atheromatous plaque. The capacity for plaque regression has recently been confirmed by serial IVUS examination in 1039 patients with stable coronary disease randomised to rosuvastatin 40 mg daily or atorvastatin 80 mg daily.[29] Atheroma volume during the 2-year monitoring period decreased by an average of about 1% in both groups, more than previously reported with less intensive statin regimens. However, additional clinical benefits of niacin have now been unequivocally ruled out in the AIM-HIGH trial in which 3414 patients with stable cardiovascular disease taking statins were randomised to receive niacin (n=1718) or placebo (n=1696).[30] Although niacin significantly increased HDL cholesterol and lowered triglycerides, differences in the primary endpoints (a composite of adverse coronary events, strokes and revascularisation) were negligible, occurring in 16% of patients in each group. The trial was stopped after an average follow-up of 3 years when it became clear HDL raising therapy with niacin was clinically ineffective. All hopes for HDL raising therapy are now invested in CETP inhibitors, and despite safety concerns following the ILLUMINATE trial of torcetrapib,[31] in which treatment was associated with increased mortality despite substantial HDL elevations, other CETP inhibitors are now entering phase III trials. A recent randomised trial of dalcetrapib in patients with acute coronary syndromes was disappointing with no reduction in the risk of recurrent coronary events despite a >30% increase in HDL levels in the treatment group.[32] An efficacy and safety trial of anacetrapib in patients with, or at high risk of, stable coronary disease was favourable, although not powered for clinical outcomes,[33] and evacetrapib has now entered the arena with a recent study showing effective HDL raising without the adverse effects on blood pressure seen with torcetrapib and, to a lesser extent, dalcetrapib.[34] Whether any of these CETP inhibitors will improve clinical outcomes, however, remains unknown.

Novel lipid-lowering drugs in clinical translation. Conventional lipid-lowering therapies, even when combined with LDL-apherisis, are often insufficient to treat to guideline targets patients with familial hypercholesterolaemia (FH), an autosomal dominant disorder of lipid metabolism associated with accelerated coronary disease.[35] There is, therefore, considerable interest in novel therapies currently under investigation, particularly lomitapide, an oral inhibitor of microsomal transfer protein and monoclonal antibodies against PCSK9. A phase II study of lomitapide in homozygous FH showed a 50% reduction in LDL-cholesterol and, although gastrointestinal side effects were common, a useful role for the drug seems likely in these homozygous patients.[36] PCSK9 inhibitors have also produced 50–60% reductions in LDL-cholesterol values in clinical studies when added to statins and ezetimibe, but unlike lomitapide, are probably mainly effective in heterozygotic FH because they act through interference with LDL receptors which are dysfunctional or completely absent in

homozygotes.[37 38] The expectation is that application of these new drugs will allow most patients with FH to achieve target concentrations of LDL cholesterol. An important component of FH management involves identification of other affected family members, and cascade screening using genetic testing has been reported as cost effective.[39] However, recent evidence suggests that polygenic disorders account for an appreciable proportion of FH cases,[40] and this will limit the effectiveness of cascade screening to relatives of mutation-positive (monogenic) cases. In other patients, with cholesterol levels consistent with an FH genotype, more conventional primary care strategies[41] should remain the screening tool of choice, at least for the time being.

REVASCULARISATION IN STABLE CAD

Percutaneous coronary intervention. The COURAGE trial was a game-changer, showing that coronary stenting in patients with stable angina did not improve cardiovascular outcomes compared with optimal medical therapy (OMT) while quality-of-life benefits were short-lived.[42 43] Now available is a meta-analysis comparing contemporary medical therapy and PCI in eight randomised trials involving 7229 patients with stable CAD.[44] Again, cardiovascular outcomes between the groups were similar during follow-up for an average 4.3 years with no significant clinical benefit for PCI, risks of death (8.9% vs 9.1%) and non-fatal MI (8.9% vs 8.1%) being nearly identical with medical therapy, while differences in unplanned revascularisation (21.4% vs 30.7%) and persistent angina (29% vs 33%) were small and insignificant. The data support recent guideline recommendations for treatment of stable angina (see above), and have been used to challenge those clinicians who continue to offer PCI to patients not receiving OMT.[45] However, FAME-II has now provided some support for an early interventional approach in a randomised comparison of OMT and PCI using drug-eluting stents guided by fractional flow reserve (FFR).[46] The study was stopped 17 months earlier than planned because the composite endpoint (all-cause mortality, non-fatal MI, urgent revascularisation) occurred in 4.3% of the PCI group compared with 12.7% of the non-PCI (OMT) group. Relief of angina was also more effective in the PCI group. Already, PCI guided by FFR has become a recommended strategy in stable coronary artery disease but some feel this is premature.[47] Thus, the treatment difference in FAME-II was driven solely by a reduction in urgent revascularisation (49 in the OMT alone group; 7 in the FFR-PCI group (HR=0.13, 95% CI
0.06 to 0.30), while the 33 deaths and non-fatal MIs were distributed fairly evenly between the groups. Moreover, the majority of patients undergoing 'urgent' revascularisation lacked objective findings of high-risk ischaemia or threshold biomarker elevations, raising concerns of biased selection of patients for invasive management during follow-up. Nevertheless, the argument in favour of interventional management as an initial strategy in stable angina has undoubtedly been strengthened by FAME-II, but final answers to the debate may have to await the findings of the ongoing International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA Trial; ClinicalTrials.gov number, NCT 01471522), comparing effects of revascularisation (PCI or CABG) combined with OMT, with OMT alone on cardiovascular death, or MI in patients with stable CAD, and objective evidence of myocardial ischaemia.

Coronary artery bypass surgery. Updated US guidelines[48] have endorsed the NICE recommendation of a multidisciplinary team approach to adjudicating revascularisation decisions in patients with complex coronary disease, encouraging application of SYNTAX and other scoring systems in arriving at an appropriate decision.[49] The potential for CABG compared with PCI to improve prognosis in patients with left main and multivessel CAD is supported by recent cohort studies,[50 51] and now available are the 5-year follow-up data from SYNTAX in which major adverse cardiac and cerebrovascular events (MACCE) were 26·9% in the CABG group and 37·3% in the PCI group, driven largely by lower rates of non-fatal myocardial infarction and repeat revascularisation for CABG, with no significant difference in all-cause mortality and stroke compared with PCI.[52] The benefits of CABG were particularly evident in patients with intermediate and high SYNTAX scores, there being no significant difference in outcomes between revascularisation strategies for patients with low SYNTAX scores. Any question about the preferred revascularisation strategy in patients with diabetes and mutlivessel coronary artery disease has now been answered by the FREEDOM TRIAL which randomised 1900 patients on OMT to either PCI with drug-eluting stents or

CABG.[53] After a median follow-up of 3.8 years, the primary outcome, a composite of death from any cause, non-fatal myocardial infarction, or non-fatal stroke, occurred in 26.6% of the PCI group and 18.7% of the CABG group. The authors concluded that CABG is superior to PCI in patients with diabetes and multivessel disease. There is less certainty about the preferred revascularisation strategy in left main coronary disease, the SYNTAX investigators reporting similar outcomes for PCI and CABG, a finding consistent with other contemporary studies that identify stenting as a reasonable strategy in appropriately selected cases, even though the need for repeat revascularisation is almost invariably higher compared with CABG.[54 55]

Surgical technique has come under considerable scrutiny recently. Concerns about the potential adverse effects of endoscopic versus open saphenous vein harvesting have been based largely on a non-randomised cohort study of 1817 patients in whom rates of vein graft failure at 1 year were 47% vs 38%, and rates of death, myocardial infarction or revascularisation at 3 years were 20.2% vs 17.4% for endoscopic versus open saphenous vein harvesting.[56] This led NICE to recommend caution in use of the endoscopic technique,[57] but such concerns have now been allayed by the results of two large cohort studies. In the US study of 235 394 Medicare CABG patients in the Society of Thoracic Surgeons (STS), national database mortality rates were similar regardless of harvesting technique, while rates of harvest site complications were lower for the endoscopic technique.[58] A UK study of 4702 CABG patients reported similar findings with no differences in in-hospital mortality (0.9% vs 1.1%, p=0.71) or midterm mortality (HR 1.04; 95% CI 0.65 to 1.66) for endoscopic versus open vein harvesting.[59]

Also under scrutiny have been the relative benefits of off-pump and on-pump CABG. Each has its proponents,[60 61] but the results of randomised outcome trials have failed to show any clear advantage for off-pump CABG, the 3-year results of the Best Bypass Surgery Trial showing no significant difference in the primary composite outcome of MACCE compared with on-pump CABG, but a tendency towards higher mortality.[62] This may reflect, at least in part, differences in graft patency rates favouring on-pump procedures, the ROOBY trial reporting rates of 91.4% vs 85.8% for arterial grafts and 80.4% vs 72.7% for saphenous vein grafts in on-pump compared with off-pump patients.[63] Particularly disappointing has been the failure of off-pump surgery to reduce cerebral injury, but a randomised comparison of minimal (MECC) versus conventional (CECC) extracorporeal circulation in 64 patients undergoing CABG has been more promising.[64] MECC was associated with improved cerebral oxygen delivery during surgery, and neurocognitive performance at 3 months was better when compared with CECC.

REMOTE ISCHAEMIC PRECONDITIONING FOR TREATMENT OF STABLE CORONARY DISEASE

Its proponents see remote ischaemic preconditioning (RIPC) as a useful and inexpensive means of improving outcomes across a range of cardiovascular disorders. They must be frustrated, therefore, by the technique's failure to penetrate clinical practice, conflicting reports of its efficacy and mechanistic uncertainty combining to undermine clinical confidence in the utility of RIPC. Some recent randomised trials have been favourable, reporting protection against contrast-induced nephropathy during cardiac catheterisation[65] and reduction in myocardial injury during heart valve surgery.[66] Perhaps the most favourable has been a randomised trial of prehospital RIPC in 333 patients with STEMI who underwent primary PCI.[67]

The group with RIPC showed a significant improvement in myocardial salvage index compared with the group without (0.75 vs 0.55) although the trial was not powered for coronary events. Against this must be set a negative trial of RIPC in a group of patients undergoing CABG,[68] but this is unlikely to be the last word, and already a meta-analysis of nine studies including 704 patients has concluded that RIPC significantly reduces troponin release during CABG.[69] Mechanistic studies of interest include one crossover study in patients with stable coronary artery disease in which RIPC reduced platelet activation during exercise testing without protecting against ischaemic ECG changes.[70] In another study of forearm blood flow using venous plethysmography in healthy volunteers, RIPC protected against impaired endotheliumdependent vasomotor function induced by ischaemia.[71] However, this protection was unaffected by infusion of a bradykinin B2 receptor antagonist, leading the authors to conclude that bradykinin is not a mediator of RIPC.

PROGNOSTIC BIOMARKERS IN STABLE CAD

Circulating biomarkers. Interest in circulating cardiovascular biomarkers has never been higher, and methodological papers have been developed to alert researchers to the standards necessary for proper evaluation of their prognostic utility.[72 73] However, a systematic review of 83 CRP studies was critical of their general quality and concluded that 'multiple types of reporting bias, and publication bias, make the magnitude of any independent association between CRP and prognosis among patients with stable coronary disease sufficiently uncertain that no clinical practice recommendations can be made'.[74] The same authors were equally critical of 19 BNP studies in patients with stable coronary disease, reporting that clinically useful measures of prediction and discrimination were generally unavailable, and concluding that the unbiased strength of association of BNP with prognosis in stable coronary disease is unclear.[75] The availability of highsensitivity assays has seen renewed interest in troponins as markers of risk in stable coronary disease, a US study of 984 patients in the Heart and Soul Study reporting that each doubling in hs-cTnT level is associated with a 37% higher rate of cardiovascular events.[76] Meanwhile the PEACE investigators have reported that among 3623 patients with stable coronary artery disease, hs-cTNI is independently associated with cardiovascular death or heart failure (HR 1.88 (1.33 to 2.66; p<0.001)), the association with non-fatal myocardial infarction being weaker
(1.03 to 2.01; p=0.031).[77] Evidence from CTCA suggests that
clinically silent rupture of non-calcified plaque with subsequent microembolisation is a likely pathophysiological mechanism of troponin elevation[78] but it is too soon to know whether it will have a clinical role in the prognostic assessment of stable coronary artery disease. The same applies to the mid-regional portion of proadrenomedullin and other biomarkers currently under investigation.[79]

Vascular biomarkers. Carotid intimamedia thickness (cIMT) is well established as a predictor of cardiovascular events in the general population and, more weakly, in patients with stable coronary artery disease.[80] Its predictive value may be enhanced by additional consideration of the extent of carotid plaque allowing derivation of the 'total burden score' which was shown by Chinese investigators to improve the prediction of the 5-year risk of cardiovascular endpoints compared with cIMT alone.[81] Certainly, the value of cIMT alone for cardiovascular risk prediction in the general population is under question following a large meta-analysis of participant-level data in 45 828 individuals in which cIMT added almost nothing to the Framingham Risk Score.[82] Further questions have been raised by another meta-analysis of participant-level data which included 36 984 individuals followed-up for an average of 7 years.[83] The investigators showed no association between progression of cIMT and risk of cardiovascular events, questioning the validity of using changes in cIMT as a surrogate endpoint in trials of cardiovascular risk.

Calcium and parathyroid hormone. Studies suggesting that people who take calcium supplements may be increasing their risk of myocardial infarction[84 85] have stimulated interest in serum calcium and its relation to cardiovascular events in patients with CHD. A recent study has confirmed that vitamin D, parathyroid hormone and calcium show association with cardiovascular risk factors in US adolescents,[86] and now we have data in 1017 patients with stable coronary artery disease followed-up for a median of 8.1 years, suggesting that high calcium levels, but not high phosphate levels, might be associated with all-cause and cardiovascular mortality (HR 2.39
to 4.66)).[87] The mechanism of this association is unclear, but the demonstration in the same cohort of a similar association between high parathyroid hormone and cardiovascular mortality may implicate calcium mobilisation from bone on the causal pathway.[88]

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Aspects anatomiques et hémodynamiques du canal artériel persistant et implications sur la fermeture percutanée

Anatomic and hemodynamic aspects of patent ductus arteriosus and implications for percutaneous closure

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Résumé

Introduction : Le canal artériel persistant (CAP) est une cardiopathie congénitale fréquente caractérisée par un shunt gauche droite et une diversité à la fois anatomique et physiopathologique. Aucune étude descriptive des variations des formes anatomique du CAP n'a été réalisée en Tunisie.

Matériels et Méthodes : Tous les patients successifs hospitalisés au service de cardiologie Sahloul en vue d'une fermeture percutanée d'un canal artériel persistant ont été inclus. Les caractéristiques cliniques et les paramètres électrocardiographiques, écho cardiographiques et surtout angiographiques ont été rapportés. Les caractéristiques morphologiques et la prévalence de chaque variante anatomique ont été décrites, ainsi que leurs conséquences sur le taux de succès et la difficulté de la technique de fermeture percutanée.

Résultats : Depuis 2005 jusqu'au mois de septembre 2013, 96 patients ont bénéficié d'une tentative de fermeture percutanée du CAP à un âge moyen de 68 ± 74 mois (extrêmes 3 mois à 32 ans) et à un poids moyen de 16 ± 12 kg (extrêmes : 4,1 à 57 kg). Selon la classification de Krichenko, le type A est la forme anatomique la plus fréquente et représente 61,4 % de l'ensemble des canaux. Le type B, C, D et E représentent respectivement 1 %, 18.8 %, 1,1% et 17,7%. Une approche transaortique a été réalisée chez 4 patients. Le taux de succès de fermeture percutanée est de 96.6 Le canal artériel n'a pas été fermé chez 12 patients en rapport avec un canal très petit dans deux cas et un canal très large chez les deux autres patients. 4 complications sont survenues et qui sont dominées par une migration de prothèse, un hématome inguinal, une protrusion de la prothèse dans l'isthme aortique dans deux cas.

Conclusion : La forme conique du canal artériel persistant est la variante anatomique la plus fréquente en Tunisie expliquant en partie le taux élevé de succès de fermeture percutanée des canaux artériels.

Mots-clés

canal artériel, anatomie, fermeture percutanée

Summary

Introduction: The patent ductus arteriosus (PDA) is a common congenital heart disease characterized by a left to right shunt and both anatomical and pathophysiological diversity. No descriptive study of anatomical variations of PDA have been conducted in Tunisia.

Methods: All consecutive patients hospitalized in the department of cardiology in Sahloul hospital for percutaneous closure of patent ductus arteriosus were included. Clinical, electrocardiographic, echocardiographic and especially angiographic features have been reported. The morphological characteristics and the prevalence of each anatomical variant have been described. Success rate and technical difficulties of percutaneous closure have been also reported.

Results : From 2005 to September 2013, 96 patients underwent attempted transcatheter closure of PDA at an average age of 68 ± 74 months (range 3 months to 32 years) and an average weight of 16 ± 12 kg (range 4.1 to 57 kg). According to the angiographic classification of Krichenko, type A is the most common anatomical shape and represents 61.4% of all PDA. Type B , C, D and E represent 1% , 18.8 %, 1.1 % and 17.7 % respectively. A transaortic approach was performed in four patients. Device implantation was successful in 96.6% of patients. Complications occurred in 4 patients.

Conclusion: Considerable variation in ductal morphology is described. The conical shape is the most common anatomic variant of PDA in Tunisia, explaining the high success rate of percutaneous closure.

Keywords

Ductus arteriosus, Transcatheter occlusion

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INTRODUCTION

La persistance du canal artériel réalise une communication entre l'aorte et l'artère pulmonaire. Les résultats encourageants et récents de la fermeture percutanée ont fait de cette technique une méthode fiable et une excellente alternative à la chirurgie (1).
La connaissance de l'aspect anatomique du CAP est primordiale avant sa fermeture percutanée conditionnant l'indication et la technique de la procédure. En effet le canal artériel se caractérise par un grand polymorphisme anatomique, morphologique et clinique (2). En 1989 Krichenco et al (3) ont mis l'accent sur l'importante variation anatomo-clinique des canaux artériels persistants et ont classé ces defects en 5 types en fonction de leur aspect angiographique respectif. A notre connaissance aucune description des aspects anatomiques et de leurs prévalences respectives n'a été rapportée en Tunisie.
Le but de ce travail est de déterminer les caractéristiques anatomiques, cliniques et hémodynamiques des patients successifs hospitalisés à l'hôpital Sahloul pour fermeture percutanée du canal artériel persistant et de préciser les implications des variations anatomiques du canal artériel sur la technique de fermeture percutanée.

MATERIELS ET METHODES

Notre étude rétrospective a inclus 96 patients successifs porteurs de canal artériel isolé et hospitalisés en vue d'une fermeture percutanée dans le service de cardiologie de l'hôpital Sahloul depuis Juillet 2005 jusqu'au mois de Septembre 2013. L'association à une communication interauriculaire et ou à une communication interventriculaire non chirurgicales n'élimine pas l'inclusion.
Les caractéristiques cliniques, échographiques et angiographiques ont été décrites chez tous les patients. Les données anthropométriques (âge de découverte, âge d'hospitalisation, le genre, le poids et la taille) ainsi que les signes fonctionnels et physiques (dyspnée, infections bronchopulmonaires à répétition, insuffisance cardiaque, présence de souffle) ont été rapportées. La présence d'hypertrophie auriculaire, d'hypertrophie ventriculaire gauche et /ou droite et l'axe du QRS ont été analysés sur l'électrocardiogramme. L'existence de cardiomégalie et des signes de congestion vasculaire pulmonaire ont été recherchés à la radiographie de thorax. Tous les patients ont bénéficié d'une échocardiographie transthoracique. Une analyse séquentielle afin d'établir le situs, les connections atrioventriculaire et ventriculoartérielle, la relations entre les gros vaisseaux, les dimensions et la fonction ventriculaire, la fonction des valves, les connections veineuses et la présence éventuelle des shunts. Le diamètre du canal artériel en mode bidimensionnelle couplé au mode couleur a été mesuré en coupe parasternale petit axe ou en coupe suprasternale. Le gradient entre l'aorte et l'artère pulmonaire à travers le canal artériel persistant est calculé grâce à l'équation de Bernouilli. La pression artérielle pulmonaire (PAP) est également évaluée par l'analyse du flux de l'insuffisance tricuspide.
Après obtention du consentement éclairé des parents des enfants ou des patients eu même lorsqu'ils sont adultes, tous les patients ont eu à la fois un accès artériel et veineux en utilisant la technique Seldinger. Un catheter d'angiographie (Pigtel, 4 ou 5 F) est positionné au niveau de l'aorte descendante distalement ou en regard de la localisation attendue du canal artériel persistant. L'angiograme initial est obtenu en projection profil en utilisant 0.5 à 1 ml /kg de produit de contraste (Hexabrix, Mal-linckrodt, Inc.) avec une vitesse d'injection à 20 ml/s. Si l'incidence profil permet de visionner correctement la forme du canal artériel, les mesures de son diamètre au niveau de l'extrémité pulmonaire, l'extrémité aortique et sa longueur sont obtenus en millimètres en utilisant le logiciel incorporé dans l'ordinateur d'analyse des images de la salle de cathétérisme. Cependant chez certains patients, l'angiographie en incidence oblique antérieur droit (OAD : 35-40°) est utilisée pour une meilleure évaluation de la forme anatomique et des dimensions du canal artériel persistant.
Le canal est mesuré sur l'angiogramme en incidence profil, où l'extrémité pulmonaire est mesurée au niveau de sa partie la plus étroite en regard de l'artère pulmonaire, l'extrémité aortique est mesurée au niveau la partie la plus large en regard de l'aorte, Sa longueur a été mesurée en dessinant une ligne du milieu de l'extrémité pulmonaire jusqu'au milieu de l'ampoule ductale. Sa forme anatomique basée sur la classification de Krichenko (3) est également évaluée. Les procédures de fermeture percutanée ont toutes été réalisées sous sédation ou anesthésie générale par voie transpulmonaire ou lorsque l'extrémité pulmonaire est très étroite par voie transaortique. Quatre types de prothèses ont été utilisés dans notre service : l'Amplatzer duct occluder I (ADO I), l'Amplatzer duct occluder II (ADO II), les prosthèses de type Occlutech PDA occluders et les coils. Toutes les complications ont été recensées. Ces complications sont de nature vasculaire (hématome, faux anévrysme), mécanique (tamponnade, perforation myocardique), rythmiques (arythmies ventriculaires), obstruction de l'artère pulmonaire et surtout aortique et migration de la prothèse.
Le recueil des données ainsi que leur analyse était effectués par le logiciel SPSS 18.0 for Windows. Les résultats étaient exprimés en moyenne et en déviation standard pour les données quantitatives et en nombre et pourcentage pour les données qualitatives. Concernant les séries de variables indépendantes, la comparaison était réalisée par le test de Chi2 pour les variables

qualitatives. Une valeur de p<0.05 est considérée comme étant significative, faisant rejeter l'hypothèse nulle.

RESULTATS

Les Caractéristiques cliniques, électrocardiographiques, radiologiques et échographiques de la population sont résumées dans le tableau n° 1.

Tableau 1:. Caractéristiques cliniquesélectrocardiographiques, radiologiques et échographiques de la population

Variables	
Nombre des patients	96
Sex ratio F/M	62/34
Age moyen au diagnostic en mois ± SD (extrêmes)	49,5 ± 53 (J1 de vie à 245 mois ? 20 ans)
Age moyen au cathétérisme cardiaque en mois ± SD (extrêmes)	68,6 ± 74 (3 à 393 mois ? 32 ans)
Poids moyen en kg ± SD (extrêmes)	16 ± 12 (4,1 kg à 59 kg)
Trisomie 21(N,%)	6 (6,25%)
Dyspnée (%)	40,6 %
Bronchite à répétition (%)	32,3 %
Insuffisance cardiaque (%)	14,6%
Souffle cardiaque (%)	83,3%
HAG à l'ECG (%)	10,4%
HVG à l'ECG (%)	37,5 %
RCT moyen ± SD (extrêmes)	0,54 ± 0,06 (0,4 à 0,7)
Congestion pulmonaire à la radiographie de thorax (%)	44,8%
Diamètre moyen du CAP (mm) ± SD (extrêmes)	4,6 ± 1,3 (2 à 9,7)
Gradient moyen à travers CAP (mmHg) ± SD (extrêmes)	74,8± 23 mmHg (10 à 110 mmHg).
PAPS > 35 mmHg, n (%)	15 (15,6 %)
Dilatation du VG (%)	60,4 %
Dilatation OG (%)	45,6 %
CIV, (N, %)	5(5,2 %)
CIA, (N, %)	3 (3,12 %)
Anomalie organique de la valve mitrale (N,%)	3 (3,12%)

CAP: canal artériel persistant, CIA: communication interauriculaire, CIV : communication interventriculaire, HAG : hypertrophie auriculaire gauche, HVG : hypertrophie ventriculaire gauche, PAPs : pression artérielle pulmonaire systolique, OG : oreillette gauche, RCT : radiographie de thorax, VG : ventricule gauche.

L'anatomie du canal artériel varie considérablement en forme et en taille (Figure n° 1). La majorité tendent à avoir une forme conique (type A). L'extrémité pulmonaire du canal mesure en moyenne 3,3 ± 1,8 mm (0,83 à 8,9 mm), l'extrémité aortique 9,2 ± 4 mm (2 à 22,36 mm) et la longueur du canal artériel 5,45 ± 3,2 mm (1,36 à 25 mm).
L'incidence profil a été initialement imagée et a permis de visualiser correctement le canal artériel dans 85 cas, cependant chez les 11 patients restants (11,46%), une incidence en oblique antérieur droit associée à une inclinaison craniale a été nécessaire pour confirmer le type anatomique du canal artériel. La forme anatomique du canal artériel déterminée par l'angiographie est la suivante : type A (n = 59, 61,4%), type B (n=1, 1%), type C (n = 18, 18,8 %), type E (n = 17, 17,7 %) et type D (n=1, 1%) (Figure n° 2). La fermeture des CAP a été assurée par une prothèse Amplatzer ADO I dans 66 cas, une prothèse ADO II dans 10 cas, une prothèse type Occlutec dans 3 cas et par coils dans 5 cas (Tableau °2).

Tableau 2 : Type de la prothèse utilisée en fonction de l'anatomie du canal artériel

	ADO I	ADO II	Occlutec	Coil	Non fermé	Total
CAP type A	50	3	1	2	3	59
CAP type B	0	0	0	0	1	1
CAP type C	12	0	2	0	4	18
CAP type D	0	0	0	1	0	1
CAP type E	4	7	0	2	4	17
Total	66	10	3	5	12	96

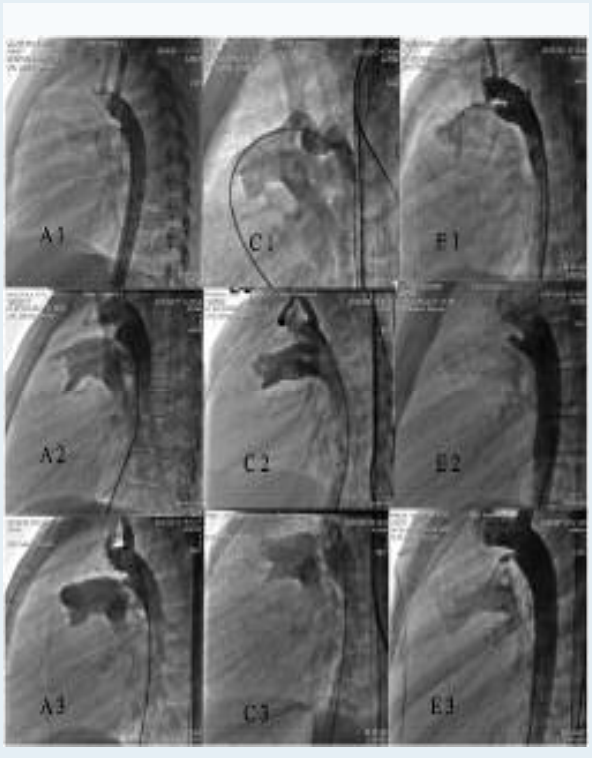

Figure 1 : Long-term survival after ASO

Le largage de la prothèse a été réalisé dans la majorité des cas (n=84, 95,4%) par voie transpulmonaire (Figure 3, Panel A). L'abord transaortique a été utilisé chez 4 patients utilisant une prothèse ADO II dans tous les cas (Figure 3, Panel B). Il s'agit de canaux de type E dans 3

cas et de type A dans un cas. L'extrémité pulmonaire est très fine inférieure à 1,65 mm dans tous les cas. Une interruption de la veine cave inférieure avec un retour veineux azygos a été diagnostiqué durant la procédure chez une fille de 17 ans motivant à changer la voie d'abord de la veine fémorale à la veine basilique droite. La procédure s'est déroulée sans incidents avec mise en place d'une prothèse Amplatzer de type ADO I de dimension 8/10 mm au niveau d'un canal artériel persistant de type A (Figure3, Panel C).

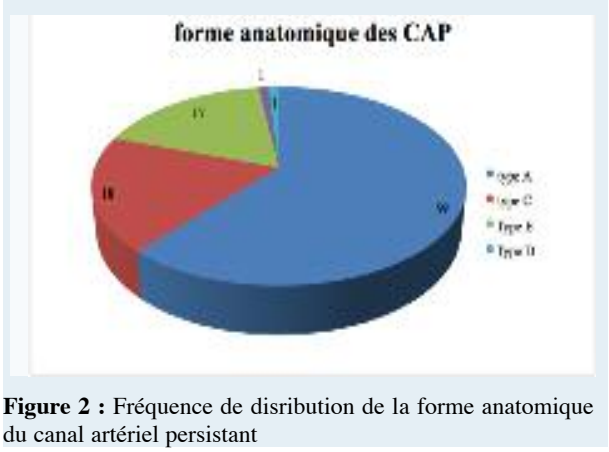

Figure 2 : Fréquence de disribution de la forme anatomique du canal artériel persistant

12 patients n'ont pas bénéficié de la fermeture de leur CAP. Le canal a été jugé d'emblée très petit dans deux cas (un de type A, l'autre de type E et très large chez deux autres (type A et C) exposant à un risque d'obstruction des structures vasculaires adjacentes particulièrement l'aorte. Chez 3 autres patients, la fermeture a échoué. Les prothèses utilisées obturant le canal artériel étaient responsables d'une obstruction aortique significative et par conséquent les prothèses ont été retirées. Le canal artériel était très compliant (de type E, C et B) et l'angiographie a sous estimé la taille de la prothèse nécessaire pour fermer le canal artériel, obligeant ainsi à utiliser d'autres prothèses plus grandes mais obstructives imposant leurs retraits. Chez les cinq patients restants, le CAP n'a pas été fermé en raison de la non disponibilité de la prothèse adéquate. Le taux de succès est estimé ainsi à 96,6% (85 CAP fermés parmi 88). Quatre complications sont survenues et qui sont dominées par une migration de prothèse (CAP type A), un hématome inguinal (CAP type E), une protrusion de la prothèse dans l'isthme aortique dans deux cas (Type E et C) responsable d'un gradient isthmique maximum de 40 mmHg dans un cas. Dans l'autre cas la protrusion a été partielle sans effet hémodynamique significatif. La prothèse de fermeture du canal a été déformée

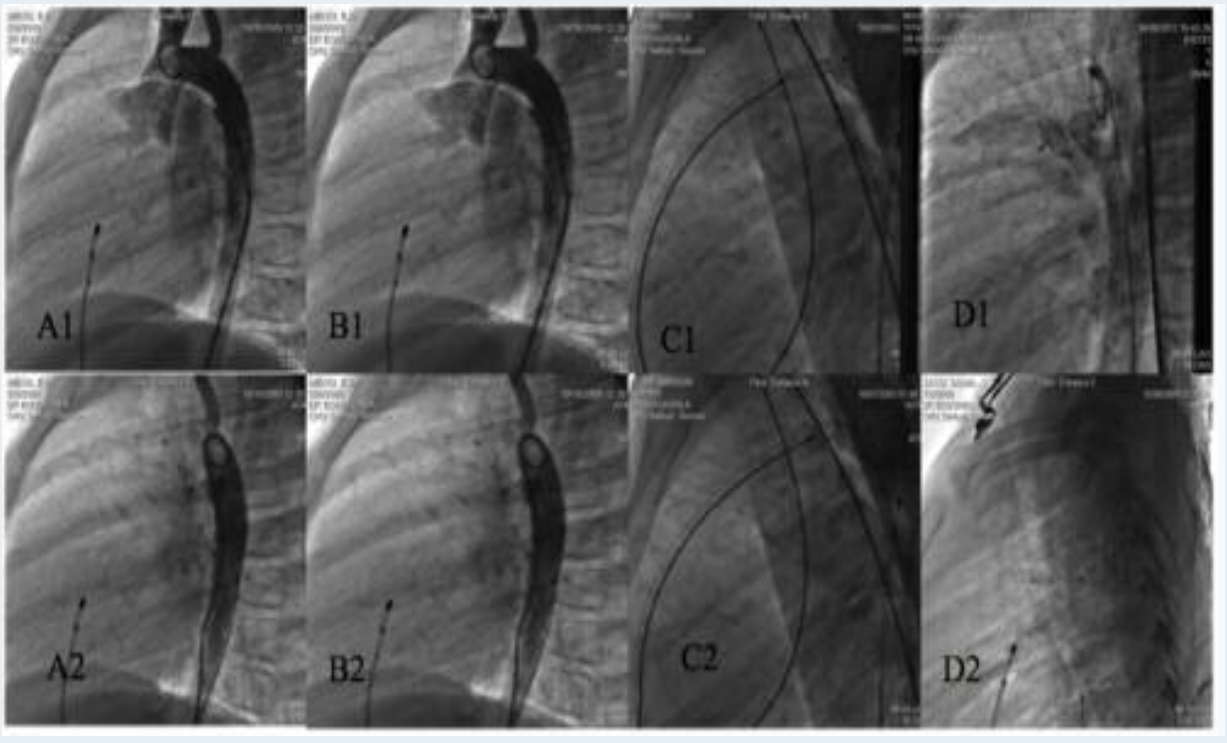

Figure 3 : Images angiographiques montrant la voie de fermeture du canal artériel persistant et l'aspect de la prothèse en fin de procédure. Panel A : fermeture d'un canal artériel de type A par voie transpulmonaire par une prothèse Amplatzer de type ADO I. Panel B : Fermeture d'un canal artériel de type A par voie transaortique par une prothèse de type ADO I. Panel C : Fermeture d'un canal artériel par voie basilique. Panel D : Déformation de prothèse de fermeture de canal artériel

angiographiquement chez deux patients en raison de la sur estimation de la taille du canal artériel (Figure n°3, Panel D). Cette déformation de la prothèse n'a pas de conséquence clinique ou échographique. Chez les 13 enfants de moins 12 mois dont 3 âgés de moins de 6 mois, la fermeture a été réalisée avec succès, sauf chez un nourrisson de 10 mois où la procédure s'est compliquée d'une migration de la prothèse imposant le recours urgent à la chirurgie cardiaque.

Il existe une corrélation entre le diamètre de l'extrémité pulmonaire et la valeur de la PAP systolique (r = 0,331 ; p= 0,005) (Figure n°4). Après ajustement sur l'âge, ce dernier n'a aucune influence sur l'association entre la PAP et le diamètre du canal à son extrémité pulmonaire.(R^2=0,103, p= 0,016).

Le type anatomique C est le plus souvent associé à une hypertension artérielle pulmonaire. Le niveau de pression artérielle pulmonaire a été comparé deux à deux entre les différentes formes anatomiques (A, C et E). La PAP systolique étant significativement plus élevée avec la forme anatomique de type C (42,3 ± 24,9 mmHg), que E (21,6±2,5 mmHg) ou A (27± 12 mmHg) (Tableau n°3). Par contre il n'y a pas de différence statistiquement significative entre la forme anatomique de type A et E. Ceci purrait être expliqué par le fait que les formes anatomiques C ont une extrimité pulmonaire plus large (Tableau n°3).

La non fermeture du canal artériel est associé à des canaux de type C (4/18) et E (4/17). Le recours à d'autres types de prothèses est également plus fréquent telle que l'ADO II, prothèse à double disque de rétention (Tableau n°2).

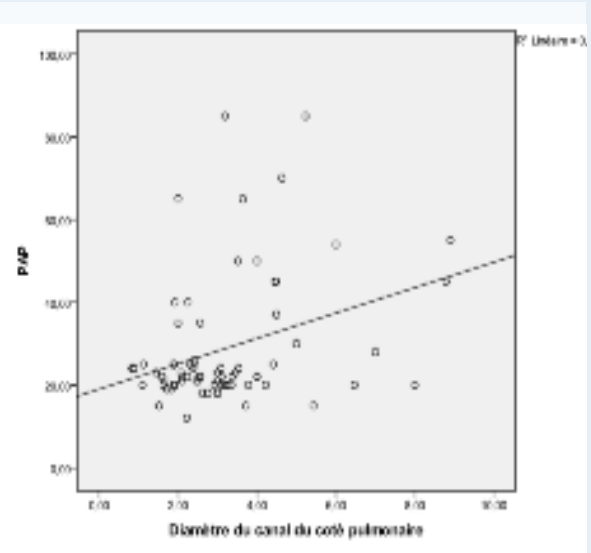

Figure 4 : Corrélation entre le diamètre de l'extrémité pulmonaire et la valeur de la PAP systolique

DISCUSSION

La prévalence de l'aspect anatomique et la taille du canal artériel persistant est variable à travers différents pays et ethnies. La forme conique est la plus commune à travers le monde mais sa prévalence varie largement entre 47 et 84 % (Tableau n°4). Les dimensions du canal sont également très variables (4). En accord avec ces résultats, une prévalence élevée des formes coniques (type A) avec une largeur moyenne de l'extrémité pulmonaire de 3,3 ± 1,8 mm est observée dans notre série. La limite principale de notre étude est d'ordre méthodologique : les patients ont été inclus de manière rétrospective sur une période de 11 ans. Cependant et grâce à l'archivage des images numériques chez tous les patients, il n'y avait aucune donnée manquante quand à l'analyse de l'anatomie et de la mesure des dimensions des canaux persistants de notre population d'étude.

Tableau 3 : Dimensions du CAP et niveau de la pression artérielle pulmonaire systolique (PAPs) en fonction de la forme anatomique.

	N	Extrémité pulmonaire moyenne ± SD (mm)	Extrémité aortique moyenne ± SD (mm)	Longueur PCA moyenne ± SD (mm)	PAPs moyenne ± SD (mmHg)	P
A	59	2,9 ± 1,33	10,4 ± 7	4,3± 1,8	27± 12	0,004*
C	18	5,5±2,05	7±2,08	7,2±5,5	42,3 ± 24,9	0,012**
E	17	2,2±0,7	8,8± 4,2	7,3± 2,1*	21,6±2,5	0,156***

Valeur de p en comparant la PAP entre A et C, ** p entre Cet E, *** p entre A et E

Bialkowski et al (8) ont comparé les aspects anatomiques et hémodynamiques du CAP chez 1404 patients vivants à haute (n= 696) ou basse (n=708) altitude. Ces auteurs ont démontré une différence de l'anatomie et de la physiologie des canaux en fonction du lieu de l'habitat. En haute altitude, les CAP sont plus larges et le niveau de pression artériel pulmonaire est plus important. En basse altitude le diamètre minimal moyen du CAP est de 2,1 mm, le type A est présent chez 50% des patients et l'incidence de fermeture par coil est de 69,2%, alors qu'en haute altitude le diamètre minimal moyen est de 4,1 mm et le type A représente 80,5 % des canaux artériels persistants et la prévalence de fermeture par prothèse d'Amplatzer de 92,5%. Les types B, C, D et E sont plus commun chez les patients vivants à basse altitude. La faible concentration en oxygène à des altitudes élevées semble jouer un rôle dans la différence de forme et de largeur des canaux. Magee et al (9) ont présenté les résultats du registre Européen de fermeture percutanée par coil du CAP incluant 1258 patients avec un diamètre minimal moyen du CAP de 2 mm. L'incidence du CAP de type A a été estimée à 43,8%. Wang et al (10) ont analysé les résultats de fermeture de 237 CAP larges à modérés avec des ADO (Amplatzer Duct Occluder), le diamètre moyen est de 4,1 mm et le type A représente 83,3% des patients. Contrairement à ces résultats, dans notre étude le type C était associé à des canaux plus larges et à un niveau plus élevé de PAP.

Bien qu'il s'agisse de la technique de référence, la détermination angiographique de la taille du canal artériel n'est pas souvent précise avant sa fermeture percutanée. L'angiographie seule ne permet pas une évaluation de la compliance du defect. Certains canaux sont très élastiques et très compliants, ce qui peut rendre difficile la fixation de la prothèse au niveau du canal artériel. Cela a été le cas chez deux de nos patients.

Le CAP est l'une des premières cardiopathies congénitales qui ont été traitées par voie percutanée (11,12). Durant les dix dernières années, l'expérience clinique de fermeture transluminale des CAP par différentes prothèses a augmenté. En 1998, l'Amplatzer duct occlude (ADO; AGA Medical Corp., MN, USA) a été introduite et est devenue la prothèse la plus fréquemment utilisée pour fermer les petits canaux ou les plus larges et apporter une solution à la quasi-totalité des formes anatomiques. Ces obturateurs en champignons, bien qu'efficace à fermer pratiquement tous les types morphologiques de PCA, semble avoir le meilleur profil pour fermer les canaux type A de la classification de Krichenko, forme la plus commune des canaux. Les recommandations actuelles suggèrent la sélection d'une prothèse dont le diamètre le plus petit est de 1 à 2 mm plus grand que le plus petit diamètre canalaire (13) et préconisent les coils pour les petits canaux de diamètre inférieur à 2 mm et les prothèses d'occlusion pour les canaux plus larges (13). La fermeture percutanée du CAP est actuellement relativement facile (14) et pose des difficultés techniques chez le nourrisson de poids inférieur à 6 kg, en cas d'hypertension artérielle pulmonaire sévère associée et en cas de petits canaux d'anatomie peu commune (type B, C et E).

De nouveaux systèmes de fermeture de plus petit calibre et de forme différente sont actuellement disponible. Les occluders sans disque de rétention tel que le nouvel amplatzer ductal occluder II, ADO II AS et les plugs vasculaires peuvent s'avérer être des outils supplémentaires utiles dans ces circonstances et répondre à la grande variété anatomique des canaux artériels (15-19). Les dernières prothèses (ADO II AS) sont proposées particulièrement en cas de petits canaux tubulaires (type C) de longueur supérieure ou égale à 3 mm et de largeur inférieure ou égale à 4 mm. Ils sont par contre à éviter pour le type B où le collet pulmonaire est plus large que le collet aortique. Ainsi la pose des coils a vu ses indications diminuées depuis ce développement technique.

Si ces techniques sont bien validées chez l'enfant et l'adulte, elles restent controversées chez le nourrisson de petit poids où le risque de complications est plus élevé. Malgré la grande disponibilité de la taille des prothèses et surtout de la taille de leur système de

Tableau 4 : Prévalence des différentes formes anatomiques du CAP à travers différents pays.

	N	A n (%)	B n (%)	C n (%)	D n (%)	D n (%)
Oho, Japan 1998 (5)	35	26 (74,28 %)	0	4 (11,4 %)	3 (8,57 %)	3 (8,57 %)
Krichenko, Canada 1989 (3)	79	51, (64.5%)	14 (17.7%)	¬(7.5%)	3 (3.7%)	3 (3.7%)
Bilkis, Malysia 2001 (6)	209	147, (71%)	0	51, (24%)	0	0
Roushdy, Egypte 2012 (7)	42	20, (47.6%)	1, (2.3%)	2, (4.7%)	2, (4.7%)	2, (4.7%)
Tunisie 2013	96	59, (61,4 %)	1 (1%)	18 (18,8%)	1(1%)	1(1%)

largage (actuellement de 4 F), la firme AGA qui commercialise la prothèse d'Amplatz a limité les indications de l'ADO aux enfants de plus de 6 mois et de plus de 6 kilos, mais de nombreuses publications rapportent son utilisation en deçà de ces limites (16,18). Dans notre étude 13 enfants étaient âgés de moins de 12 mois dont 3 sont âgés de moins de 6 mois. La procédure s'est déroulée avec succès sauf chez un enfant âgé de 10 mois où la procédure s'est compliquée d'une migration de la prothèse.

Les séries de Butera et al (20) et de Fisher et al (21) soulignent les difficultés qui peuvent être rencontrées chez le petit enfant. Les complications liées à l'abord vasculaire sont d'autant plus fréquentes que l'enfant est petit. Pour réduire le taux des complications locales, Godart (23) propose de ne pas faire d'abord artériel : l'aortographie peut être réalisée par une sonde passant à travers le canal artériel, et le positionnement de la prothèse peut être contrôlé par une échographie transthoracique. La progression du matériel peut être difficile, en raison des angles « aigus » qu'il doit franchir dans les cavités droites, qui peuvent être responsables d'un « king-king » de la sonde. L'existence d'un angle aigu entre le canal et l'aorte ou l'absence d'ampoule aortique peuvent être responsables d'une protrusion du disque de la prothèse dans l'aorte, et donc d'une obstruction aortique. Deux solutions sont proposées: l'ouverture du disque de la prothèse dans le canal – la prothèse doit alors mettre en tension les parois du canal pour éviter le risque d'embolisation à droite – ou l'utilisation d'autres types de prothèses à double disque (ADO II ou ADO II AS) (16-18).

La fermeture de canaux larges avec hypertension artérielle pulmonaire sévère reste problématique. Chez des patients sélectionnés avec une pression artérielle pulmonaire supérieure à 60% de la pression systémique, des obturateurs Amplatzer de communication interventriculaire ou interauriculaire sont utilisés pour minimiser le risque d'embolisation de la prothèse liée à une rétention par un disque unique (23-26).

CONCLUSION

La connaissance de l'aspect anatomique du CAP est primordiale avant sa fermeture percutanée conditionnant l'indication et la technique de la procédure. En effet le canal artériel se caractérise par un grand polymorphisme de ses aspects anatomiques, morphologiques et cliniques. La forme conique de canal artériel est aussi dominante en Tunisie.

Le taux de succès de la fermeture percutané est élevé et le taux de complication est faible. Le type anatomique C est le plus souvent associé à une HTAP. Le taux d'échec est associé à des canaux larges de type C et E.

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CARDIOLOGIE TUNISIENNE

ARTICLE ORIGINAL

Determinant factors of long term outcome after arterial switch for transposition of the great arteries in Tunisian children.

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Summary

The arterial switch operation (ASO) has become the surgical technique of choice for correction of TGA since it allows not only establishment of normal pulmonary and systemic circulations, but also establishment of subnormal anatomy with particularly a sub aortic morphologically left ventricle. Nevertheless, long term complications may occur. This study aims to reveal long term complications after this type of surgery and to analyze their determinant risk factors.

It's a retrospective analysis including patients who underwent an ASO for TGA between April 1992 and July 2007 and continued to be followed in our department of Pediatric Cardiology at Rabta hospital, Tunis. The inclusion criterion was at least 5 years follow-up.

The survival probability at 10 years was of 97.7%. Mildly reduced fraction of shortening (FS) was found in 5 patients (11.36%). One patient had an impaired left ventricular function with antero-septal wall hypokinesia due to an occlusion of the proximal LAD.

RVOT obstruction was found in 6 patients (13.63%) and was severe in 2 patients. Freedom for RVOT obstruction was 90% and 77%, respectively, at 10 and 15 years after ASO. Pulmonary regurgitation (PR) was frequent (40.90%), Freedom from neoaortic valve regurgitation was 75% at 5 years, 60 % at 10 years and 52 % at 15 years after ASO . Risk factors identified as predictors of this AR were VSD , aortic coarctation , 2-stage repair , native pulmonary valve regurgitation and immediate postoperative AR . Coronary lesions were found in 4 patients (9.09%) requiring a coronary artery bypass graft (CABG) in 1 case. No ischemic mitral regurgitation was observed and no patient underwent percutaneous coronary intervention during follow-up. Intramural coronary artery course was the risk factor of late coronary arteries lesions.

In our study freedom from late reintervention was 92% at 10 years and 84% at 15 years after ASO. Four patients (9.09%) underwent 7 late reoperations at a mean age of 10.46 years. reoperations were related to the RVOT (57.14%)

In conclusion, ASO offers good long term prognosis. The association to a VSD was not considered to be a predictor of long-term complications except of aortic regurgitation. Right ventricular outflow tract dysfunction was the main reason for late reinterventions. Potential risk of myocardial ischemia requires regular appropriate investigations.

Keywords

Transposition of the great arteries, Arterial switch operation, long term, risk factors

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INTRODUCTION

Transposition of the great arteries (TGA) is the most common cyanotic congenital heart disease in neonates. After its introduction by Jatene and colleagues in 1975, the arterial switch operation (ASO) has become the surgical technique of choice for correction of TGA since it allows establishment of both circulations in series with a systemic ventricle of left morphology avoiding the risk of systemic ventricular dysfunction, encountered frequently with atrial Switch procedures previously used. Although this technique represents the best hope for durable and normal survival, long term complications may occur.

Our study aimed to assess the long term results of ASO in Tunisian children with TGA and to identify potential factors affecting these results.

PATIENTS AND METHODS

We performed a retrospective analysis including patients who underwent an ASO for TGA between April 1992 and July 2007 and continued to be followed in our department of Pediatric Cardiology at Rabta hospital, Tunis. Clinical and demographic characteristics were collected for all patients. The surgical anatomy was recorded at the time of surgery and the anatomy pattern coded based on mode of origin, course and branching pattern of the coronary arteries, as described by Yacoub and Radley-Smith [1].

The inclusion criterion was at least 5 years follow-up.

In total, 44 patients were included. Table 1 shows demographic and clinical characteristics of the population. The median age was 11.55 ± 4.23 years [5.0–20.0 years] and median follow up was 8.83 ± 4 years [5.0–20.0 years].

Table 1: Demographic and clinical characteristics of the patients.

Demographic parameters		
Age	Years	11,55 ± 4,23
Female	n	12 (27%)
First treatment		
Rashkind atrioseptostomy	n	27 (61.36%)
Prostaglandin infusion	n	27 (61.36%)
Surgical anatomy		
TGA with IVS/VSD	n	22/22
Aortic coarctation	n	4 (9.09%)
Coronary pattern (A/B/C/D/E)	n	29/3/2/6/4
intramural course	n	2 (4.54%)
pulmonary bicuspid valve	n	5 (11.36%)
aortic bicuspid valve	n	1 (2.27%)
Surgical details		
Age at ASO	days	65,38 ± 60,87
Weight at ASO	g	3889 ± 924
Two- stage repair	n	5 (11.36%)
Extracorporeal circulation	mn	135 ± 28
Lecompte maneuver	n	43 (97.72%)
Difficulty in coronary transfer	n	5 (11.36%)

Complete clinical examination, standard and 24 hours Holter electrocardiogram (ECG), echocardiography and were performed in all patients and coronary investigations were available in 50% of the cases. Symptoms were graded according to the New York Heart Association functional class (NYHA) classification.

Statistical analysis:

We analyzed data with STATISTICA (version .10). Univariate analysis of nominal variables thought to affect mortality or occurrence of late complications or reoperations was done with the χ^2 or Fischer exact test, when appropriate. The level of significance was set at $p<0{\cdot}05$. Survival probability and freedom from events were calculated by the Kaplan-Meier method.

RESULTS

Late mortality :

During the follow-up period, 1 patient (2.27%) died at the age of 7 years. This corresponds to a survival probability of 97.7% at 10 years after the ASO. This patient had a pacemaker for postoperative AVB (TGA with VSD). He was asymptomatic at the latest assessment. The death was due to a septic shock. A pacemaker endocarditis was suspected but not confirmed.

Symptoms and functional status:

Most patients reported a normal exercise tolerance (90.91% in NYHA class I), while 9.09% were in NYHA class II. Atypical chest pain was present in 6 patients (13.63%). Five patients reported palpitations (11.36%) but no syncope was observed.

Ventricular function:

The majority of patients had a normal fraction of shortening (86.36% with FS > 33%). Mildly reduced fraction of shortening (FS) (between 27% and 33%) was found in 5 patients (11.36%). One patient had an impaired left ventricular function with antero-septal wall hypokinesia due to an occlusion of the proximal LAD. The improvement of LV function was noted after surgical revascularization by coronary artery bypass grafting (CABG).

A significant difference in LV systolic function was found between patients who had undergone a 2-stage repair compared to those with a one stage repair and between patients who had undergone an early ASO (≤ 28 days) and those operated on later (respectively p=0.049 and p=0.01). No significant difference was found between patients with or without VSD (17/22 vs 21/22, p=0.23)

Right ventricular outflow tract (RVOT) outcome :

RVOT obstruction, defined as a right ventricle-pulmonary artery (RV-PA) gradient ≥ 25 mmHg was found in 6 patients (13.63%) and was severe in 2 patients. The

Table 2: Details of late RVOT complications

Age of ASO (days)	NYHA	RV-AP gradient (mmHg)	level of RVOT obstruction	Reoperation	Age of reoperation (years)
14	II	70	multiple	Enlargement of Pulmonary artery trunk and branches	19
25	II	100	valvular + subvalvular	Resection of the pulmonary valve and a hypertrophic muscle bar + transannular patch.	2.5

pulmonary stenosis (PS) was valvular in 4 patients, combined valvular and subvalvular in 1 patient and was present at multiple levels in 1 patient. Freedom for RVOT obstruction was 90% and 77%, respectively, at 10 and 15 years after ASO. Two patients (33.33%) underwent one or more interventions due to RVOT obstruction. Table 2 provides clinical details of these two patients.

No significant difference in the risk of RVOT obstruction was found between patients with or without a ventricular sepal defect (VSD) and between patients with or without aortic coarctation (respectively, p= 0.44 and p=0.4).

Pulmonary regurgitation (PR) was frequent (40.90%), and was moderate or severe in 2 patients. One late reoperation was necessary for a severe regurgitation due to pulmonary valve resection for RVOT obstruction (table 2).

Outcome of the neoarta :

Neoaortic root dilation appeared in 16 patients (36.36%) during follow-up. At least mild aortic valve regurgitation (AR) was present in 20 asymptomatic patients (45.45%). Freedom from neoaortic valve regurgitation was 75% at 5 years, 60 % at 10 years and 52 % at 15 years after ASO (figure n°2).

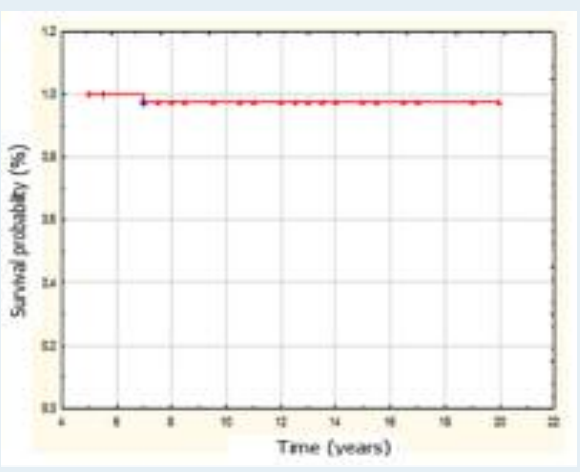

Figure 1 : Long-term survival after ASO

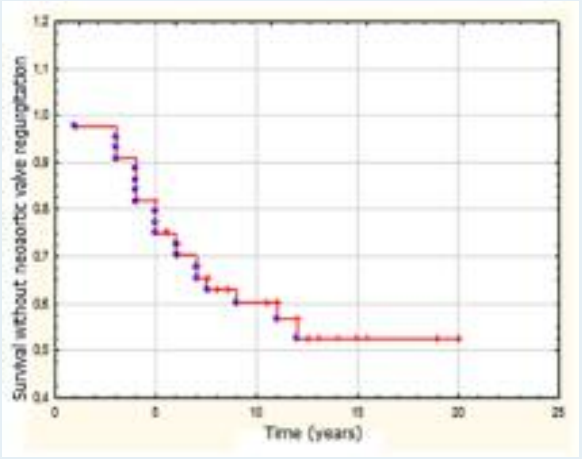

Figure 2 : Freedom from neoaortic regurgitation after ASO

Risk factors identified as predictors of this AR were VSD (p= 0.02), aortic coarctation (p=0,038), 2-stage repair (p=0.04), native pulmonary valve regurgitation (p=0.04) and immediate postoperative AR (0,048). At last follow-up, none of the patients in the cohort had required reoperation on for neoaortic root dilation or neoaortic valve regurgitation.

Stenosis of the aortic valve or anastomosis did not occur. One patient (TGA with VSD) had a severe subaortic stenosis due to a redundant patch. He required reoperation 7 years later for thpatch. VSD patch replacement by a smaller one.

Coronary complications:

Information on the coronary pattern, as documented at the time of ASO, was available in all patients (figure n°3). Intramural coronary artery course was observed in 2 patients and operative difficulties in coronary reimplantation were reported in 5 patients. However, during the follow-up, the coronary imaging was performed in only 50% of case (22 patients) at a mean age of 10.48 years. A coronary angiography was indicated in first intention in 1 case because of instable angina. In 4 cases, the coronary angiography was performed after a

CT coronary scan and in 17 cases the CT scan was sufficient. Coronary lesions were found in 4 patients (9.09%) requiring a coronary artery bypass graft (CABG) in 1 case. Table 3 shows details about these 4 cases of coronary lesions. No ischemic mitral regurgitation was observed and no patient underwent percutaneous coronary intervention during follow-up.

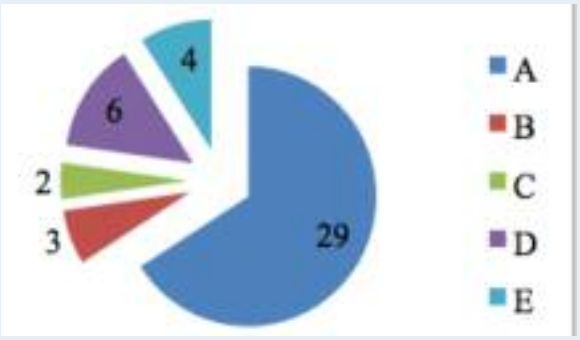

Figure 3 : Coronary anatomy distribution following Yacoub and Radley Smith Classification

Freedom from coronary artery complications was 87.5% at 10 years and 72% at 15 after ASO (fig.4). Intramural coronary artery course was the risk factor of late coronary arteries lesions (p=0.013) (table 3).

Table 3 : Predictors of late coronary complications

	Coronary complications (4)	p
TGA + VSD	3	0,11
Intramural course	1	0,013
Réimplantation difficulties	1	0,2
Coronary anatomy		0,7
A	3	
B	0	
C	0	
D	0	
E	1	

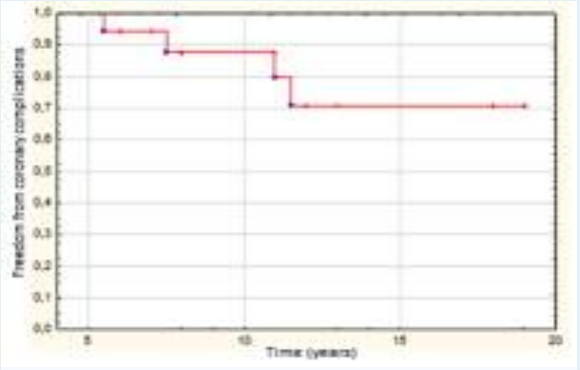

Figure 4 : Freedom from coronary complications after ASO

Arrhythmia and conduction abnormalities:
Three patients presented a post-operative 3rd degree atrioventricular block (AVB) requiring pacemaker implantation and later battery replacement. Sustained ventricular tachycardia occurred in one case with LAD proximal occlusion with no relevant arrhythmias observed after surgical revascularization.

Late reinterventions :
In our study freedom from late reintervention was 92% at 10 years and 84% at 15 years after ASO (figure n°5). Four patients (9.09%) underwent 7 late reoperations at a mean age of 10.46 years. The indications were as follows: pulmonary stenosis (n=2), RVOT reconstruction (n=2), CABG (n=1), aortic stenosis (n=1), recoarctation (n=1). The most common causes of late reoperations were related to the RVOT (n=4, 57.14%) and only one late reoperation for coronary complication was required.

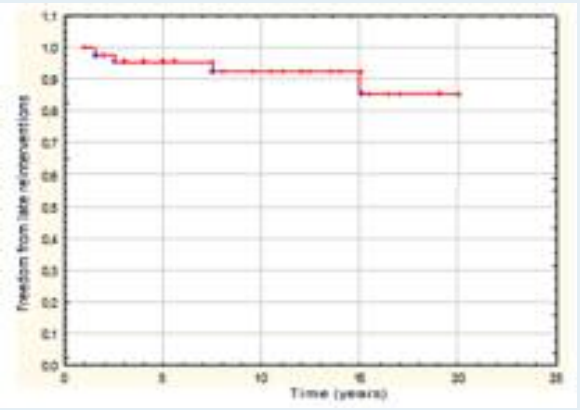

Figure 5 : Freedom from late reoperations after ASO

COMMENT

The ASO is the treatment of choice of TGA because it restores a normal anatomic connection of the ventricles to the great arteries TGA [2]. The initial enthusiasm for the ASO was tempered by the high mortality during the early years [3]. Gradually, short- and mid-term results were promising, but data on long-term outcome are limited. As anticipated, long term complications such as coronary disease, aortic root dilatation, valvular dysfunction, and need for RVOT interventions remained an issue during childhood and beyond [4,5].

Late mortality :
Late mortality has been limited to 1 patient (2.27%) and survival probability was 97.7% at 10 years after the ASO. This mortality rate in is comparable to that reported in other studies [6,7].

The association to a VSD seems not to be a risk factor for late mortality [8,9]. Patients with low operative weight and who underwent ASO beyond the neonatal period, although exposed to a greater early mortality, have substantially the same long-term survival [10]. The most common cause of late mortality is related to coronary problems, followed by RVOT dysfunction [6].

Symptoms and functional status:
Long-term physical performance after ASO is excellent. Physical and aerobic capacities are significantly higher than after atrial switch [11,12]. Importantly, exercise ability is comparable to healthy children [13].
The chronotropic response to exercise is often impaired [14]. This may be related to the self denervation as in cardiac transplantation [14]. Kondo and al showed evidence of sympathetic denervation in the early postoperative period, with different degrees of nerve regeneration 5 years after surgery [16]. Abnormal response to circulating neurohormones, such as endothelin-1, was also observed in a study with a small number of patients after ASO [17]. The cardiac output during exercise, is usually normal [14]. Regular monitoring of the physical performance seems justified because of the improvement in life expectancy after ASO with active teenagers and young adults even aspiring to sports competition.

Ventricular function:
A severely reduced LV function was rare (2.27%) in our cohort. The cause was related to myocardial ischemia and a significant improvement of LV function was obtained after surgical revascularization. However, the longitudinal and diastolic functions were not assessed in our study.
In Pettersen and coworkers compared a group of 22 patients who underwent ASO for TGA to a second group of 22 age-matched healthy subjects considered as controls. They were investigated by magnetic resonance imaging (MRI) and echocardiography. Myocardial deformation was described by longitudinal, circumferential shortening and ventricular torsion, measured by speckle-tracking echocardiography. Although standard measurements of global systolic LV function were normal in patients with TGA, longitudinal shortening was decreased compared with controls. Longitudinal strain was decreased in all ventricular regions except the posterior wall and most pronounced in the apical segments. LV circumferential shortening was similar in the 2 groups. Moreover, LV torsion was decreased in the TGA group [18]. A recent study of Grotenhuis and coworkers, conducted with cardiac MRI in the 16th year of follow-up after ASO, showed an impaired global systolic function corresponding to the long term development of an initially subclinical myocardial [19].

In our study, a better LV function was related to an early ASO and a 2-stage repair and no significant difference was found between patients with or without VSD. Myocardial ischemia and a lack of adequate myocardial protection represent two important reasons which can be responsible for an impaired LV function.

RVOT outcome:
Despite various techniques of reconstruction of the neopulmonary root, late development of supravalvular PS remains the most frequent complication and cause of reoperation after the ASO for TGA [20,21,22]. In our study, a PS was observed in 6 cases (13.64%) requiring late reoperation in 2 cases. Yamaguchi and coworkers have suggested that the development of PS occurs progressively [23]. Williams and coworkers reported an increase in the rate of reoperation for PS after ASO from 8% at 7.6 years to 13.8% at 16 years in the same group [24]. In our cohort, the probability of survival without RVOT obstruction at 10 years was 90% and 77% at 15 years after ASO. The most incriminating factors are related to the surgical technique. PS is often due to an inadequate growth of the new pulmonary tract and a circumferential fibrosis of the stitches area. Moreover, an inadequate Lecompte maneuver can cause tension in the stitches area responsible later for a pulmonary gradient [25]. Some complex anatomical forms of TGA are thought to be associated with a higher risk of RVOT obstruction such as TGA with VSD or aortic coarctation and "side to side" great arteries presentation [26]. No significant relationship was found between these factors and RVOT obstruction in our study.
From a therapeutic point of view, stenosis of the pulmonary artery trunk and branches are often treated by percutaneous dilation and covered stents [27]. Surgery can be indicated, as a first line therapy, in complex lesions or in case of percutaneous procedure failure.
Data on PR after arterial switch operation are limited. Its incidence hugely varies from 6 to 50 % in literature [28,29]. This high incidence remains surprising compared to the low incidence of aortic native valve. On the other hand, moderate PR may be observed in healthy children [30]. This suggests that a low pressure system may predispose to a lack of coaptation of pulmonary semi-lunar valves. This PR is always moderate with no hemodynamic changes and no need for reoperation. One patient in our cohort required RVOT reconstruction for an important PR due to a previous pulmonary valve resection.

Outcome of the neoarta:
AR is a common complication after ASO. According to reported series, its onset is often early with an incidence varying from 30 to 50% after 5 years [31,32]. However, it rarely causes hemodynamic disturbances and

exceptionally requires late reoperations [33]. This finding would suggest that progressing neo-aortic valve dysfunction is not a major issue in intermediate and long term follow-up. In our study, freedom from AR was 75% at 5 years, 60 % at 10 years and 52 % at 15 years after ASO.
The aortic root was found to be dilated in 16 patients (36.36%). The fact that no patient required aortic root replacement suggests that aortic dilatation is not rapidly progressive.
Aortic stenosis is a rare complication which remains stable during follow-up with no need for late reoperations.

Coronary complications:
Coronary lesions are the most common cause of late mortality after ASO [34]. The anatomic repair technique requires a transfer of the coronary arteries from the aorta to the proximal pulmonary artery (neo-aortic root). Complications can be related to the variability of coronary anatomy before transfer [35]. Some situations, such as intramural course and coronary anatomy type B are predictive of coronary lesions [36]. However, the mechanism of such complications has not been well explained in the vast majority of cases with apparently favorable coronary anatomy (A or D).
In these patients, the anatomical relationship between the reimplanted coronary arteries and the great arteries were suspected [37]. Ou and coworkers found that an anterior position of the left coronary artery was the main characteristic of patients with obstruction of LMC or LAD. They hypothesized that this anterior position led the proximal portion of the left coronary artery around the aorta and potentially pass between the aorta and the pulmonary artery [38].
An intramural course represented in our study the only predictor of late coronary lesions. The symptoms are usually mild or absent (silent ischemia). The majority of reported complications occurred during the first year after ASO [39] and coronary events become rare after 5 years [40].
On basis of these data, we recommend coronary investigations in the following situations: in case of clinical, electrical or echocardiographic signs of myocardial ischemia; during the first year after ASO for complex coronary anatomy models and/or in case of difficulties in coronary transfer; systematically at the age of 5 years and at the end of the growth period.
Coronary angiography is indicated if myocardial ischemia is observed. Otherwise, a coronary CT scan is performed. The percutaneous angioplasty has recently shown good mid-term results [41] but CABG, using left internal mammary artery, feasible in most children, remains the most widely used technique [42].

Arrhythmia and conduction abnormalities:
In our study, one case of ischemic VT was noted. The outcome was favorable after surgical revascularization. No other cases of sustained arrhythmias were observed. Myocardial ischemia should always be discussed and coronary investigation should be indicated.

Late reoperations :
According to literature, RVOT complications are the most frequent cause of late reinterventions [43]. Four late reinterventions were performed because of RVOT dysfunction in our cohort. Coronary complications represent the second cause [44]. Fricke and coworkers found that association to VSD or to aortic coarctation represents a risk factor for late reoperation [45]. Two other factors were identified: the resection of LVOT obstacle at the same time of ASO and a long circulatory arrest [45]. In our study freedom from late reoperation was 92% at 10 years and 84% at 15 years.

CONCLUSION

The TGA, including complex types, can be corrected with good long-term outcomes by ASO. The association to a VSD was not considered to be a predictor of long-term complications except of aortic regurgitation. Right ventricular outflow tract dysfunction was the main reason for late reinterventions. Potential risk of myocardial ischemia requires regular appropriate investigations. We strongly recommend complete and regular follow-up in specialized centers even in adulthood.

Study limitations
This current study was designed to assess complications of patients who survived to 5 years after ASO. Therefore we cannot comment on early outcomes or mortality in childhood. In addition, we did not assess temporal changes of ventricular function, the longitudinal and diastolic functions of the LV and the right ventricular function. -The coronary anatomy was coded according to the Yacoub and Radley-Smith classification at the time of operation and we employed this system later during the study. Other classification systems have been developed and may have yielded slightly different results such as Marie Lannelongue classification [46].
- Coronary investigations were available only in 50% of patients. Thus, the prevalence of anatomical coronary problems may be underestimated. For logistical reasons, we could not perform cardiopulmonary exercise testing for our cohort. Therefore, these data are incomplete and prone to selection bias.
As a first experience in Tunisia, further studies are required for a more detailed assessment of the left and right ventricular functions, exercise capacity or quality of life in this population.

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Cardiac events during the Costello syndrome. About one case and review of the literature

Evénements cardiaques durant le syndrome de Costello.

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Summary

Costello syndrome is a rare syndrome associated with de novo mutations in the HRAS gene. It's mostly revealed during in the first months of life by growth retardation, facial dysmorphic features, skin and cardiac abnormalities and subsequent cognitive deficit of varying severity. We report a case of Costello syndrome in a 3 month old infant. The initial cardiac investigations were normal except frequent premature atrial complexes. After few months, worsening arrhythmia with bursts of ventricular tachycardia were noted as well as the secondary progressive obstructive left ventricular hypertrophic cardiomyopathy (HCM).

Cardiac involvement is determinant for the prognosis of Costello syndrome. It frequently consists of hypertrophic cardiomyopathy (one third of patients), with involvement of the left ventricle in half of the cases. It is often asymmetrical and associated with obstruction of the outflow recalling family hypertrophic cardiomyopathy. The natural history of HCM in Costello syndrome and its management remains poorly known because of paucity of reported cases. Progression of the HCM can be very rapid like the reported case. On the other hand, the spontaneous regression of the HCM in some patients has been reported. In addition, cardiac threatening arrhythmias may be noted. So that, cardiac assessment and monitoring with regular echocardiography and electrocardiogram follow up is mandatory.

Keywords

Cardiac, hypertrophic cardiomyopathy, arrhythmia

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INTRODUCTION

Costello syndrome is a rare syndrome associated with de novo mutations in the HRAS gene. The prevalence of this syndrome is unknown, but about 250 cases have been reported in the literature [1]. We report the case of an infant with Costello syndrome with severe cardiac events and we present a brief review of literature on the characteristics of cardiac involvement in this syndrome.

OBSERVATION

We report the case of a 03 month old male infant. His parents were concerned about swallowing disorders with loss of weight of 900 grams in one month. The medical history revealed severe hydramnios, macrosomia with a birth weight of 4700 grams and neonatal hypoglycemia and hypocalcemia. The infant had a weight of 4300 grams at his first presentation. Physical examination revealed facial dysmorphism suggestive of Costello syndrome with macrocephaly (head circumference of 41.5 cm so -3 SD), epicanthus, strabismus, flattened nose, low-set ears, macroglossia and short neck (Figure1).

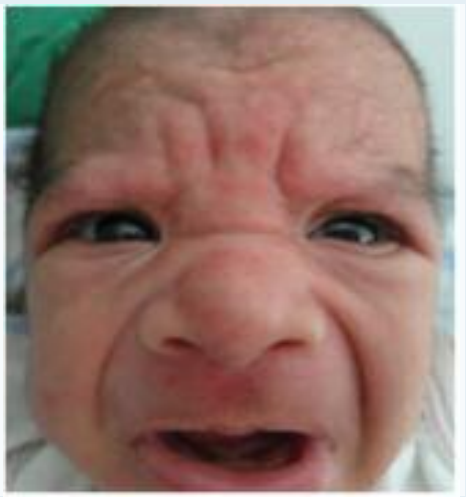

Figure 1 : Dysmorphic features suggestive of Costello's syndrome.

The infant also had skin abnormalities and hair and nail characteristics of Costello syndrome: Cutis laxa (Figures 2a and 2b), deep folds of the palms and soles (Figures 3a and 3b), laxity of small joints of the hand and axial hypotonia. Psychomotor development and growth of our patient were marked by poor gain of weight, short stature, delayed psychomotor acquisitions and poor coordination sucking - swallowing.

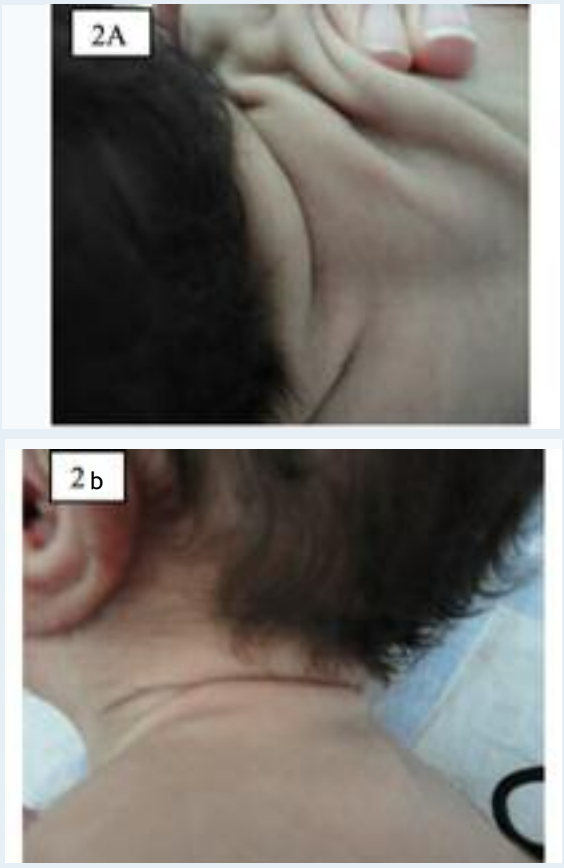

Figure 2 : (2A et 2B) : Cutis Laxa features

A genetic study confirmed the diagnosis of Costello syndrome.

On cardiovascular routine examination, the heart rate was around 140 beats per minute. Blood pressure was 80/40 mm hg and cardiac auscultation was normal. The femoral pulses were well felt and there was no sign of heart failure. The electrocardiogram showed a regular sinus rhythm with some premature ventricular contractions (PVCs). The initial echocardiogram was normal. In particular, there was no evidence for a cardiomyopathy or septal defect and the heart valves were thin and healthy. The ECG Holter monitoring showed frequent PVCs sometimes in doublets associated to few bursts of premature atrial complexes. The infant was then started on beta blockers and close monitoring was recommended.

Three months later, echocardiographic study showed an asymmetric non obstructive hypertrophic cardiomyopathy involving especially the basal part of the ventricular septum measured at 9 mm. There was no left ventricular outflow obstruction or mitral regurgitation. Left

ventricular function was preserved and pulmonary pressures were normal. The ECG Holter monitoring objectified repetitive PVCs in doublets and triplets with ventricular tachycardia bursts (Figure 4). We decided to add amiodarone to the beta blocker treatment.

Figure 2 : (2A et 2B) : Cutis Laxa features

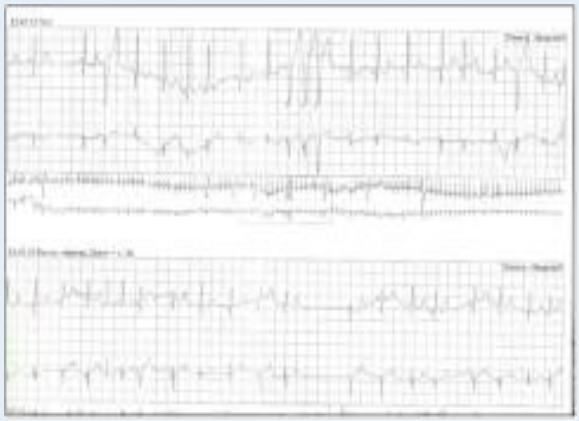

Figure 4 : Repetitive premature ventricular complexes.

The evolution was marked by the disappearance of ventricular tachycardia bursts, and a scarcity of PVCs. The infant was asymptomatic cardiac wise and swallowing disorders are relatively improved, thanks to a rehabilitation of swallowing. However, echocardiographic assessment done three months later showed a worsening of HCM with septal thickness of 10 mm, thickened mitral valve with onset of moderate mitral regurgitation, as well as a left ventricular outflow tract obstruction with a peak gradient of 40 mm Hg measured 2 months later at 64 mm Hg (Figures 5- 6).

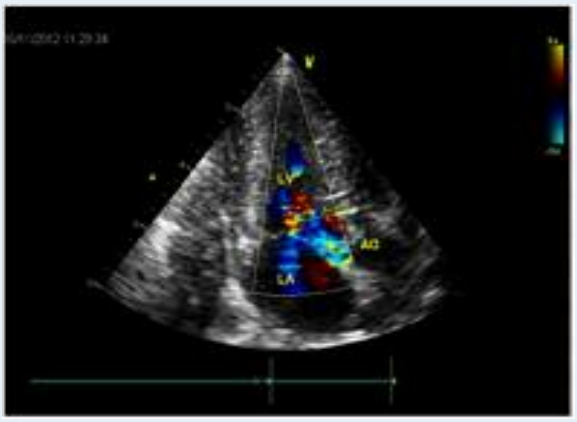

Figure 5 : Apical view showing moderate mitral regurgitation and acceleration of the flow over the sub aortic region .

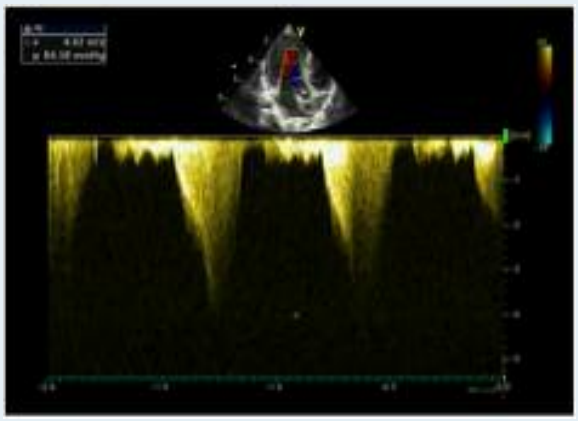

Figure 6 : Peak gradient of 64 mm Hg over the left ventricular outflow tract.

DISCUSSION

Costello syndrome was first described in 1971 by Costello [2]. The gene responsible for this syndrome is the HRAS gene [3]. Diagnosis is mainly clinical. In the series published by Lin and al about 61 genetically confirmed cases of Costello syndrome, the average age at diagnosis

was 4.2 years. The diagnosis was made before the age of 1 year in one third of cases [4]. Clinical presentation consists on facial dysmorphism, growth retardation associated with severe psychomotor retardation and feeding difficulties [5]. A notion of polyhydramnios during pregnancy, macrosomia and neonatal hypoglycemia are often found [6]. Prognosis is dependent on frequent development of tumors, essentially rhabdosarcomes neuroblastoma on one hand and on the cardiac involvement on the other hand [4]. The most common reported heart lesions are pulmonary stenosis, hypertrophic cardiomyopathy, cardiac arrhythmias, atrial or ventricular septal defects (44%) and congenital mitral valve abnormalities [7]. Dysmorphia and cardiac involvement of Costello syndrome are similar to those of Noonan syndrome, cardio-facial-cutaneous syndrome (CFC) and LEOPARD syndrome. These syndromes are due to mutations in genes that encode proteins involved in the intracellular cascade of RAS / mitogen-activated protein kinase (MAPK). They are also called "RASopathies" [3].

The prevalence of HCM in Costello syndrome varies from 20 to 61% depending on the series [4, 7]. In the series of Swiwik et al [7], the age of discovery of the HCM ranged from 5 months to 20 years. Similarly, Lin et al [4] noticed that the diagnosis of HCM is not always done at birth. Indeed, some patients develop HCM later, as is the case of our patient. This could be related to myocardial accumulation of metabolites over time [8]. Regular echocardiographic monitoring is necessary because for the possibility of rapidly evolving forms of HCM as in the case of our patient.

HCM in Costello syndrome is similar to familial forms of HCM. Symptoms usually described are dyspnea, angina, syncope, arrhythmias and sudden death. The hypertrophy of basal part of the ventricular septum is the most common [9]. Severe hypertrophy and left ventricular out flow obstruction and may be cause of dyspnea or angina on exertion. Life-threatening ventricular arrhythmias are possible. At histological analysis, hypertrophy, myocyte disorganization and fibrosis, which represent the anatomical substrate of ventricular arrhythmias, were identified in the HCM Costello syndrome [8].

Resolution or significant spontaneous regression of the septal hypertrophy has been interpreted as a phenomenon of widespread remodeling leading to raise the hypothesis that the HCM associated with Costello syndrome is not a static disease [4]. Moreover, a rapidly fatal evolution with a rapid enhancement of the left ventricular gradient and occurrence of heart failure signs has been reported in the literature [10].

To improve the quality of life of these patients, medical intervention and / or surgery may be necessary to reduce the degree of obstruction and reduce complications such as arrhythmias [11].

Supraventricular tachycardia, especially atrial tachycardia is frequently associated with Costello syndrome (up to one third of patients). The first cases of Costello syndrome associated to supraventricular rhythm disturbances have been reported in 1993 [12].

Then Siwik et al [7] described the cardiac manifestations of Costello syndrome in 30 patients, 18% had tachyarrhythmias. It was ectopic atrial tachycardia, supraventricular tachycardia of unspecified mechanism and a case of flutter. In the series published by Lin et al [13], one third of children had arrhythmias, 74% in type of atrial tachycardia. The other children had ventricular arrhythmias in type of premature ventricular complexes or well tolerated neonatal ventricular tachycardia. Our infant had impaired ventricular excitability with bursts of ventricular tachycardia, which have well resolved on anti arrhythmia drugs.

CONCLUSION

Costello syndrome is a rare genetic syndrome. Clinical expertise and molecular study allow the diagnosis of this disease. Cardiac involvement, particularly hypertrophic cardiomyopathy and rhythm disorders, alters the prognosis. Their possible rapidly fatal progression imposes a close cardiac rhythm monitoring and echocardiography follow up.

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Embolie pulmonaire massive mimant un infarctus du myocarde antéro-septal

Massive pulmonary embolism mimicking an anteroseptal myocardial infarction

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Résumé

Malgré les progrès récents le diagnostic de l'embolie pulmonaire reste encore difficile à établir. Dans certaines situations les données cliniques et les manifestations électrocardiographiques peuvent orienter le diagnostic vers celui d'un infarctus du myocarde. Nous rapportons le cas d'une embolie pulmonaire massive chez un patient de 50 ans. L'ECG initial a montré un sus-décalage transitoire du ST en antéro-septal. Le diagnostic d'un syndrome coronarien aigu a été alors retenu. Néanmoins l'échocardiographie faite en urgence a montré un cœur pulmonaire aigu et l'angioscanner thoracique a confirmé le diagnostic d'embolie pulmonaire proximale bilatérale. La coronarographie a montré un réseau angiographiquement sain.

Mots-clés

Embolie pulmonaire ; Infarctus du myocarde ; ECG ; Sus-décalage du segment ST.

Summary

Pulmonary embolism remains the major malingerer of acute chest disease. The clinical and electrocardiographic manifestations may deviate to a diagnosis of myocardial infarction. We report a case of massive pulmonary embolism in a patient of 50 years. The electrocardiogram showed a transient ST elevation in anteroseptal leads. The diagnosis of acute coronary syndrome with transient ST segment elevation was retained. Echocardiogram showed a acute pulmonary heart and thoracic CT angiography confirmed the diagnosis of bilateral proximal pulmonary embolism. The coronary angiography was normal.

Keywords

Pulmonary embolism; Myocardial infarction; ECG; ST elevation

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INTRODUCTION

L'embolie pulmonaire est une maladie fréquente et grave. Les signes cliniques de l'embolie pulmonaire ne sont pas suffisamment sensibles ni spécifiques pour que le diagnostic puisse être éliminé ou affirmé sur la seule foi de l'interrogatoire et de l'examen clinique [1, 2].
Dans le but de contourner cette difficulté, des algorithmes décisionnels à but diagnostique ont été proposés par les sociétés savantes [3].

Les signes à électrocardiogramme (ECG) évocateurs d'une embolie pulmonaire ont été bien identifiés. Parmi eux, le sus décalage du segment ST est en revanche rare. Il traduirait une souffrance ischémique du VD secondaire à une embolie pulmonaire grave [6, 7].
Nous rapportons le cas d'une embolie pulmonaire considérée initialement à tort comme un infarctus aigu du myocarde.

OBSERVATION

Il s'agit d'un patient âgé de 50 ans tabagique à 30 PA sans autres facteurs de risque cardiovasculaires qui a consulté aux urgences à H1 d'une douleur médio-thoracique constrictive associée à une dyspnée. L'examen physique était sans anomalie. L'ECG fait à H1 du début des douleurs (Figure n°1) a montré une tachycardie sinusale à 110 bpm, un axe du QRS à 80°, un sus-décalage de ST de 2 mm en V1-V2, bloc de branche droit incomplet et une onde p pulmonaire.

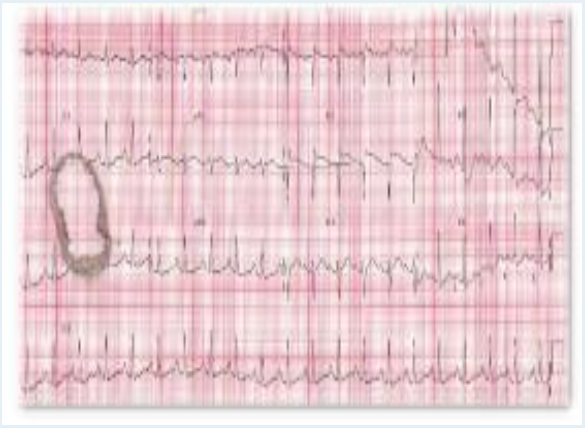

Figure 1 : ECG à l'admission

Le diagnostic de syndrome coronarien aigu a été retenu dans un premier temps et le malade a reçu de l'aspégic, du clopidogrel et de l'héparine. Une thrombolyse a été envisagée mais non faite après constatation de la régression rapide du sus-décalage du segment ST.

Le diagnostic d'un syndrome coronarien aigu avec sus-décalage de ST transitoire a été quand même retenu. Toutefois la coronarographie (Figures n°2 et 3) faite dans les 24 heures a révélé un réseau angiographiquement sain. L'échocardiographie transthoracique faite en urgence qui avait montré un ventricule gauche non dilaté de cinétique normale et une dilatation des cavités droites avec un septum dyskinétique a permis d'évoquer à postériori le diagnostic d'embolie pulmonaire.

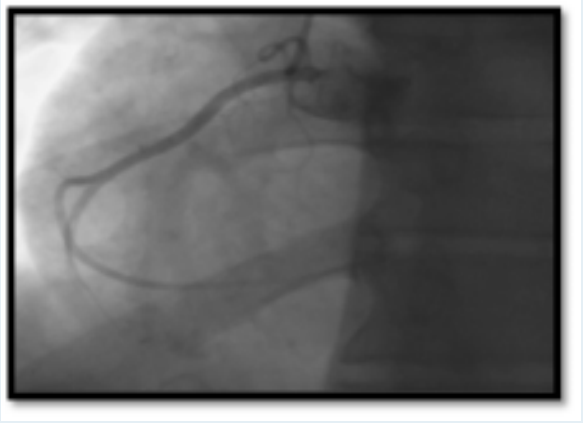

Figure 2 : La coronaire droite en OAG cranial

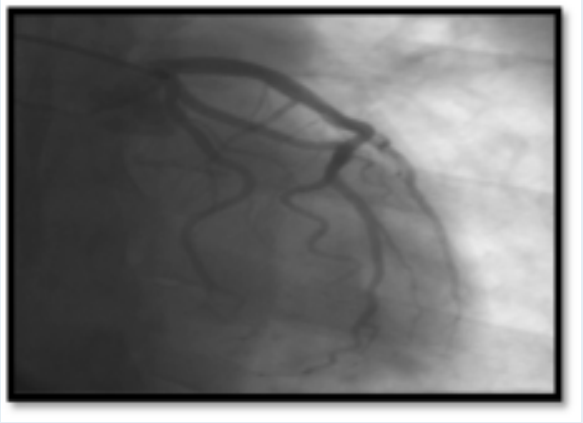

Figure 3 : Réseau gauche en OAD caudal

Un angioscanner thoracique (Figure n°4) a alors confirmé la présence d'une embolie pulmonaire proximale bilatérale.
L'échographie doppler veineux des membres inférieurs n'a pas retrouvé de thrombose veineuse profonde.

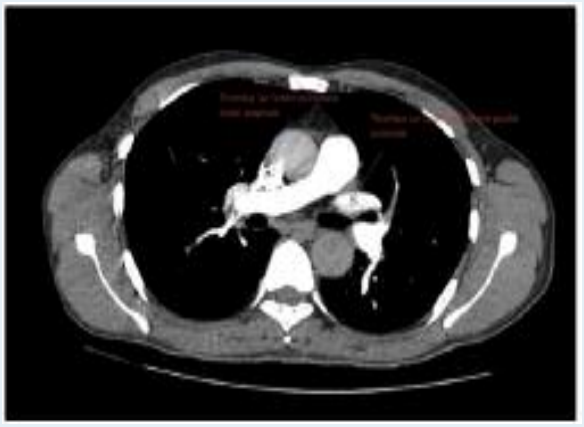

Figure 4 : Angioscanner thoracique avec le temps d'injection des artères pulmonaires

En l'absence de retentissement hémodynamique, une thrombolyse intraveineuse n'a pas été indiquée et l'évolution sous traitement anticoagulant à dose curative a été rapidement favorable avec disparition des anomalies cliniques, échographiques et électriques (figure 5)

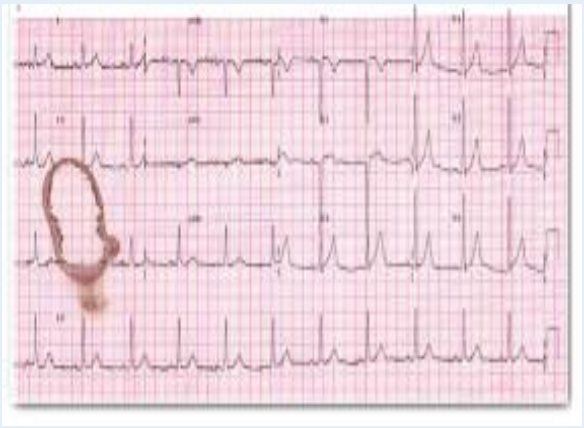

Figure 5 : ECG après traitement anticoagulant

Normalisation de l'ECG après traitement anticoagulant à dose curative
L'enquête étiologique étant négative, la décision fut de prescrire un traitement anticoagulant oral par antivitamine K sur une durée prolongée supérieure à un an.

DISCUSSION

La démarche diagnostique de l'embolie pulmonaire repose sur une présomption anamnestique, clinique, gazométrique et électrocardiographique. La confirmation est souvent apportée par l'angioscanner thoracique. De nombreux scores ont été établis pour faciliter l'approche diagnostique de l'embolie pulmonaire tels que les scores de Wells[8] et de Genève[9]. Malgré l'existence de ces scores, le diagnostic de l'embolie pulmonaire demeure difficile[10]. La douleur thoracique qui est fréquente peut faire penser à tort à un syndrome coronarien. C'était le cas de notre patient dont la douleur avait les caractéristiques d'une douleur d'origine angineuse en rapport avec une ischémie du VD.
Les manifestations électrocardiographiques associées à l'embolie pulmonaire ont été bien décrites dans la littérature médicale. Mais elles manquent de sensibilité et de spécificité. Ces anomalies incluent la tachycardie, la déviation axiale droite, le bloc de branche droit incomplet, l'aspect S1Q3T3, les ondes T négatives en antéro-septal, l'onde p pulmonaire et parfois même un passage en fibrillation auriculaire aiguë [11].
Rodger et al. ont étudié les observations de 246 patients atteints d'une embolie pulmonaire. Ils ont constaté que seuls la tachycardie sinusale et le bloc de branche droit incomplet étaient significativement plus fréquents dans les populations de patients présentant une embolie pulmonaire[5].
De même, Sinha et al. Après avoir analysé les ECG de 270 patients (130 avec embolie pulmonaire prouvée et 140 patients dans le groupe témoin) ont conclu que la tachycardie sinusale (39%vs 24 %), le S1Q3 (12%vs 3 %), la tachyarythmie atriale (15%vs 4 %), la présence d'une onde Q en DIII (40% vs 26%) étaient des signes électriques significativement associés à l'embolie pulmonaire[4].
Sukhia et al. ont étudié les ECG de 190 patients et en ont aussi relevé que l'association d'au moins deux des cinq critères suivants (S1, Q3, S1Q3, tachycardie sinusale et tachyarythmie supraventriculaire) a une sensibilité de 78% et une spécificité de 96% [12].
Des modifications du segment ST ont été également rapportées notamment le sus-décalage dans les dérivations droites [6, 7] [13]. Dans notre cas, le sus-décalage siégeait dans le territoire antéro-septal et était associé à des signes électrocardiographiques évocateurs d'embolie pulmonaire comme le bloc de branche droit et l'onde p pulmonaire.
Plusieurs hypothèses ont été avancées pour expliquer ces anomalies du segment ST [14]:
une ischémie myocardique fonctionnelle du ventricule droit secondaire à une augmentation de la demande en oxygène du fait de la tachycardie et de l'inotropisme accru et de l'élévation de la tension pariétale suite à la

dilatation du ventricule droit[15].
une ischémie mécanique : compression coronaire par la dilatation ventricule droit ou pressions élevées dans l'oreillette droite entravant la vidange du sinus coronaire.
un spasme coronaire secondaire à l'hypoxie ou une embolie paradoxale au niveau coronaire.
L'infarctus du ventricule droit est un diagnostic différentiel à évoquer. Le sus-décalage de ST peut être constaté en V1, V2 en plus des dérivations droites V3R, V4R.
Ce cas clinique plaide en faveur de la réalisation d'une échocardiographie précoce devant tout syndrome douloureux thoracique en particulier lorsque le diagnostic de syndrome coronarien aigu (SCA) n'est pas certain. De même dans certaines situations cliniques comme la nôtre la présence d'un sus décalage du segment ST doit faire aussi évoquer l'éventualité d'une embolie pulmonaire souvent proximale. Toutefois la réalisation d'une échographie cardiaque ne doit retarder la prise en charge du patient notamment une exploration coronarographique et un éventuel geste de revascularisation associé si le diagnostic final était celui d'un SCA.
Conclusion : L'embolie pulmonaire peut simuler un syndrome coronarien aigu. En effet dans un contexte de douleur thoracique aiguë la présence d'un sus-décalage du segment ST peut orienter à tort vers le diagnostic d'infarctus du myocarde. Cette situation clinique est certes rare mais doit être envisagée en cas de tableau atypique. C'était le cas de notre patient. En cas de doute la démarche diagnostique devrait incorporer une échographie cardiaque en urgence afin d'orienter le choix l'examen ultérieur de confirmation du diagnostic soit vers l'angioscanner thoracique soit vers la coronarographie.

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Le retour veineux pulmonaire anormal total : deux présentations cliniques d'une même pathologie

Total abnormal venous connection: twos clinical presentations for the same disease

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Résumé

Le retour veineux pulmonaire anormal total (RVPAT) est une cardiopathie rare. Il est souvent responsable de manifestations cliniques bruyantes chez les nouveaux nés. La majorité de ces enfants meurent avant l'âge de 1 an en l'absence de correction chirurgicale. Nous rapportons dans ce qui suit trois cas de RVPAT dans ses deux formes supra et infra cardiaque. La présentation clinique était typique chez deux nouveaux nés contrastant avec une pathologie bien tolérée chez un enfant de 6 ans.

Mots-clés

cardiopathie congénitale, retour veineux pulmonaire anormal, insuffisance cardiaque, scanner multibarette

Summary

The total abnormal venous connection (TAPVC) is a rare heart disease. It is often responsible for severe clinical manifestations in neonates. The majority of these children die within the first year of life in the absence of surgical correction. Herein, we report three cases of RVPAT in its two forms supra and infracardiac. The clinical presentation was typical in two newborns contrasting with a well-tolerated in 6 years old child.

Keywords

congenital heart disease, total abnormal venous connection, heart failure, multidetector computed tomography

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INTRODUCTION

Le retour veineux pulmonaire anormal total (RVPAT) est une cardiopathie congénitale rare. Il représente 1% du total des cardiopathies congénitales (1). Tout le sang veineux pulmonaire provenant des quatre veines pulmonaires est drainé anormalement dans l'oreillette droite, le sang est ensuite distribué dans la circulation systémique par le biais d'un shunt auriculaire droit-gauche obligatoire. Deux éléments conditionnent la présentation clinique : la taille de la communication auriculaire et la présence éventuelle d'une obstruction du retour veineux.

Les patients atteints de RVPAT bloqué sont symptomatiques immédiatement après la naissance et sont souvent cyanosés. Les patients avec RVPAT non bloqués sont souvent asymptomatiques à la naissance, la moitié de ces patients développent des symptômes au cours du premier mois de vie et la majorité décèdent au cours de leur première année de vie en l'absence de chirurgie(2). La chirurgie sans délai apparait donc comme un traitement de choix dès que le diagnostic est fait(2).

La survie après l'âge de 1 an est exceptionnelle. Nous rapportons ici trois cas récemment pris en charge de RVPAT (2 supra et un infra cardiaque). Nous insistons sur le contraste qui existe entre les deux premiers cas où le diagnostic est fait avant 1 mois et le troisième cas où le diagnostic est fait à l'âge de 6 ans.

Premier cas :

Un nouveau-né de sexe masculin de 35 jours a été adressé au service de pédiatrie en mai 2011 pour absence de prise de poids et polypnée constatées lors d'une visite de routine. L'examen physique a révélé l'absence de prise pondérale avec un poids à 3kg500, une polypnée à 60 cycles/min avec tirage sous costal. L'auscultation cardiaque a révélé une tachycardie avec un éclat de B2 et un bruit de galop. La palpation abdominale a retrouvé une hépatomégalie à un travers de doigt. Les pouls fémoraux et huméraux étaient présents et symétriques.

La radiographie du thorax a montré une cardiomégalie avec une surcharge pulmonaire bilatérale. L'échographie cardiaque (figure 1) a montré un ventricule droit très dilaté avec des pressions pulmonaires iso-systémiques avec courbure septale plate et ventricule gauche écrasé. Le sinus coronaire était dilaté témoignant de la présence d'une veine cave supérieure gauche (VCSG). Les quatre veines pulmonaires semblaient se jeter dans un collecteur derrière l'oreillette gauche lui-même drainé dans la VCSG très dilatée. Un angio-scanner réalisé aussitôt a confirmé le diagnostic de RVPAT dans la VCSG (figure 2).

L'enfant a été opéré à l'âge de 2 mois avec fonte de la paroi postérieure de l'oreillette gauche avec le collecteur. Le suivi régulier a montré un enfant en bon état de santé avec normalisation des données échographiques

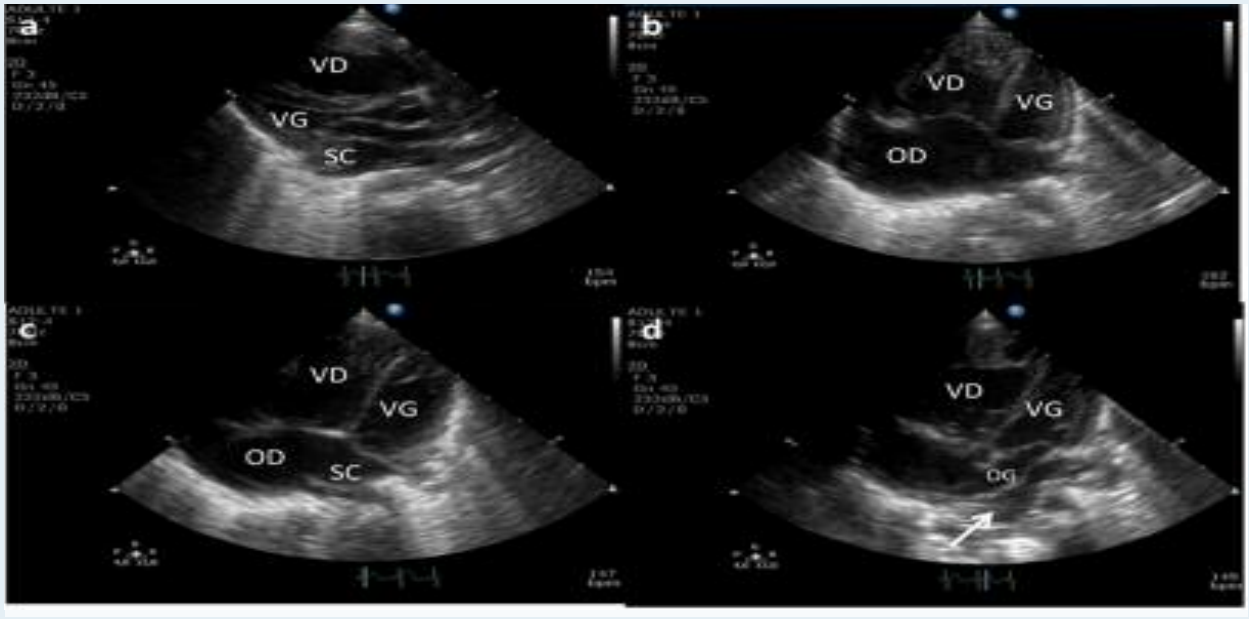

Figure 1 : (a) coupe echographique parasternale grand axe montrant un VD dilate et un sinus coronaire dilate.(b)coupe apicale 4 cavités montrant une petite OG et une OD dilatée.(c) la coupe 4 cavités tronquées en post permet de dégager un sinus coronaire dilaté.(d)le collecteur se situs derrière l'OG et reçoit les 4 veines pulmonaires

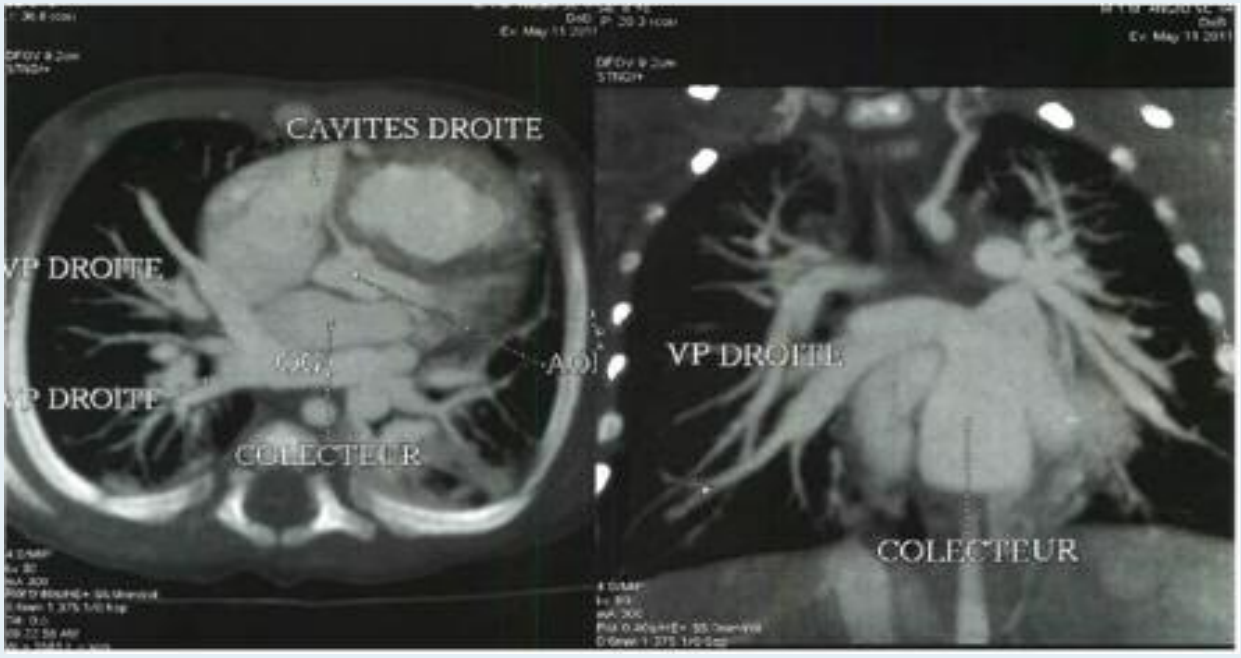

Figure 2: Aspect du RVPAT au scanner avec les 4 veines pulmonaires se jetant au niveau de la veine cave superieure gauche

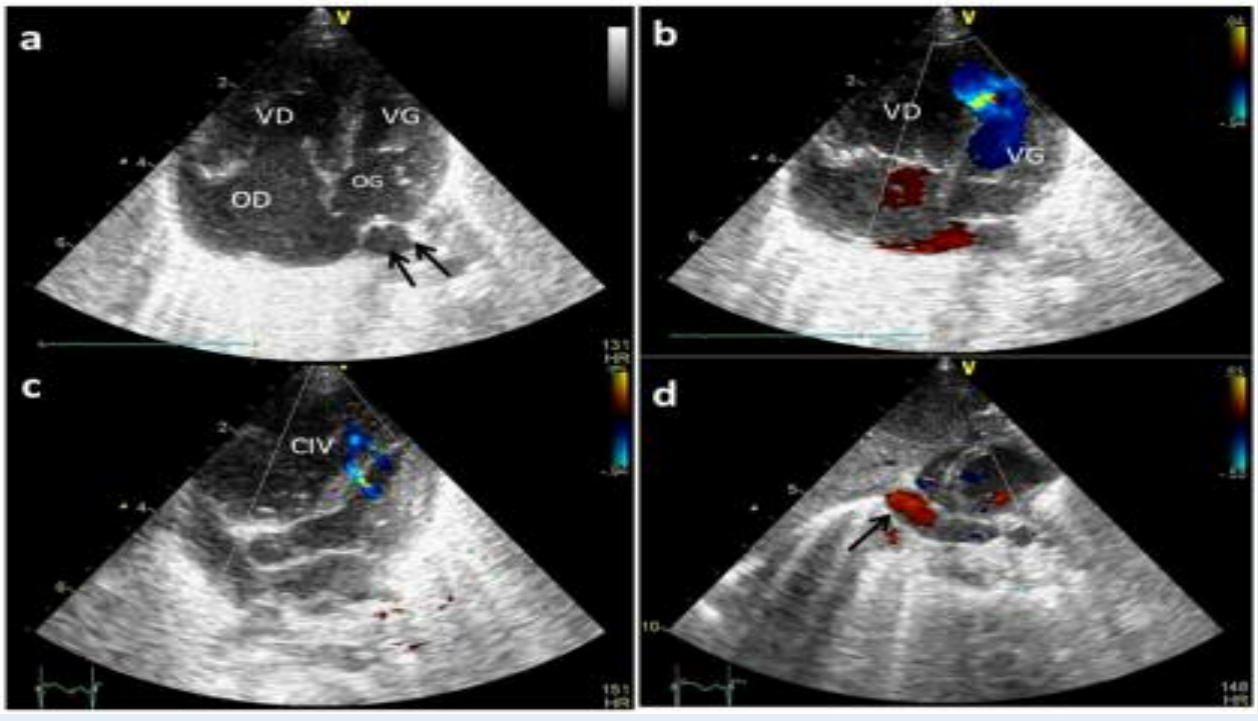

Figure 3:(a)coupe 4 cavités montrant un VD et une OD dilatés, une petite oreillette gauche et le collecteur situé derrière l'oeillette gauche.(b et c)coupe 4 cavités montrant deux CIV à shunt droit gauche.(d)la flèche indique la veine de drainage avec un flux se dirigeant vers le foie.

Deuxième cas :
Un nouveau-né de sexe féminin âgé de 20 jours a été ramenée aux urgences en février 2013 par ses parents pour dyspnée et difficultés alimentaires. L'examen physique a révélé l'absence de prise pondérale avec un poids qui était identique au poids de naissance. Une tachypnée avec des signes de lutte respiratoire a été notée. L'auscultation cardiaque avait montré une tachycardie sans bruit surajoutés. L'ECG a montré un rythme sinusal, axe droit et une onde R exclusive en V1 avec des ondes T positives en V1, V2 et V3. La radiographie du thorax a montré une surcharge pulmonaire sans image de foyer. L'échographie cardiaque (figure 3) a révélé la présence d'un collecteur derrière l'oreillette gauche qui reçoit quatre veines pulmonaires et qui est drainé à travers une veine de drainage dans une veine infra-diaphragmatique.
Le ventricule droit était très dilaté avec des pressions pulmonaires élevées.
Deux petites communications inter-ventriculaires de 5 et 2 mm ont été visualisées avec un shunt droit-gauche.
Un angio-scanner thoracique a confirmé le diagnostic et a précisé un drainage de la veine de drainage dans le tronc porte (figure 4).
L'indication opératoire était portée mais la petite fille est décédée 4 jours après le diagnostic.

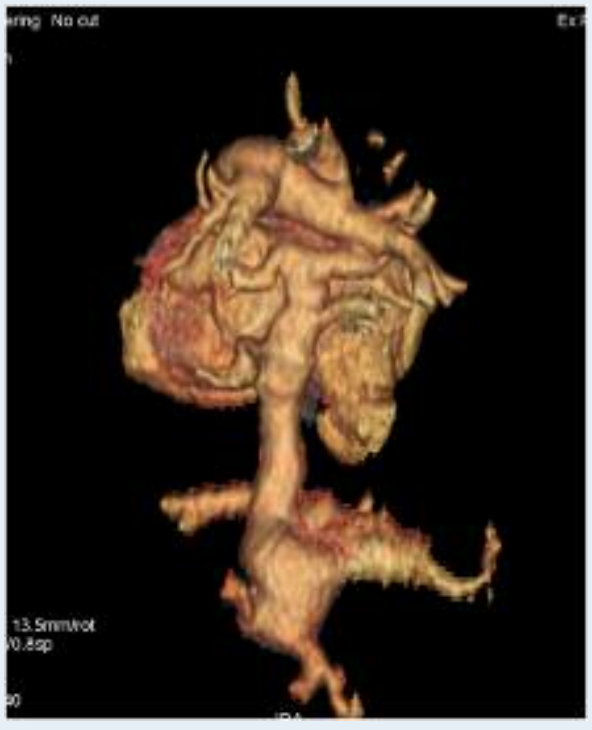

Figure 4 : reconstruction scannographique montrant les 4 veines pulmonaires se jettant au niveau du collecteur puis drainées par la veine de drainage dans le tronc porte.

Troisième cas :
Un garçon de 6 ans a été référé à notre centre en octobre 2011 pour prise en charge d'une communication inter-auriculaire. Le patient se plaignait de dyspnée d'effort. L'examen physique montrait un enfant eutrophique avec un bon développement staturo-pondéral. L'auscultation cardiaque a révélé un souffle systolique au foyer pulmonaire avec dédoublement fixe de B2. La palpation abdominale était normale. Il n'y avait pas de cyanose apparente mais la saturation en O2 était de 89% à l'air ambiant.
L'ECG a montré un rythme sinusal avec des signes d'hypertrophie ventriculaire droite et un bloc de branche droit. La radiographie du thorax a montré une cardiomégalie modérée et des signes de surcharge pulmonaire. L'échographie cardiaque (figure 5) a montré une dilatation importante du ventricule droit non concordante avec la présence d'une petite communication inter-auriculaire avec shunt droit-gauche. Les veines pulmonaires étaient drainées dans un collecteur situé derrière l'oreillette gauche, une large veine de drainage se jetant dans la veine cave supérieure a pu être visualisée. Un angio-scanner était réalisé pour mieux définir l'anatomie des veines pulmonaires a confirmé le RVPAT supra cardiaque dans la veine cave superieure droite.
L'enfant était opéré avec succès. Un suivi régulier de l'enfant a montré une récupération de la taille du ventricule droit avec des pressions pulmonaires normales.

DISCUSSION

Le RVPAT est une cardiopathie congénitale rare et ne représente que 1% des cardiopathies congénitales(1). Il existe quatre types de RVPAT selon le site de drainage (3). Le type 1 est de loin le plus fréquent (3) avec un drainage supra cardiaque (c'est le cas des observations 1 et 3).
La présentation clinique était typique dans les deux premiers cas avec un tableau franc d'insuffisance cardiaque. Cette présentation clinique contrastait avec la 3ème observation où le diagnostic était fait inhabituellement à l'âge de 6 ans. Le diagnostic après l'âge de 1 an est rare. Dans la série de Gathman et al. (2) parmi 75 patients avec RVPAT, 6 patients uniquement étaient diagnostiqués après l'âge de 1 an.
Le diagnostic de RVPAT a été fait même après 40 ans chez 3 patients dans la littérature (4). Ce type d'anomalie peut être un véritable défi pour un cardiologue adulte et peut être facilement diagnostiqué à tort comme une large communication inter-auriculaire comme chez notre patient de 6 ans. Une petite oreillette gauche sans flux veineux pulmonaire associé à un shunt droit gauche atrial doit soulever de tels soupçons.
Le contraste qui existe dans la gravité des tableaux

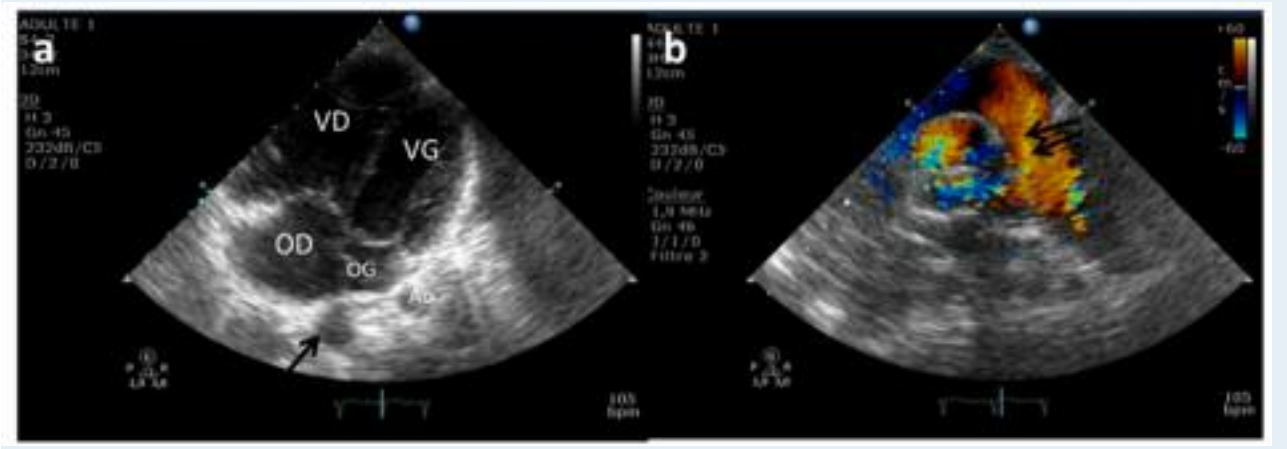

Figure 5: (a) Coupe 4 cavités montrant un VD dilate, une petite oreillette gauche derrière laquelle existe une structure vasculaire différente de l'aorte et qui correspond au collecteur.(b) La veine de drainage montrée par deux flèches et qui se jette dans la veine cave supérieure droite.

reste, cependant, intriguant. Une large communication inter-atriale et l'absence d'hypertension artérielle pulmonaire pourraient être chez notre grand enfant à l'origine de la bonne tolérance de la maladie. En effet, ces facteurs ont été largement soulevés dans la série de Gathman(2) avec un meilleur pronostic et moins d'insuffisance cardiaque dans le groupe sans HTAP. L'HTAP, quand elle existait, a été expliquée en partie par une obstruction au niveau des veines pulmonaires, mais certains patients avaient développé une HTAP même en l'absence d'obstruction des veines pulmonaires. Ainsi, il semble qu'il y ait d'autres facteurs qui font qu'un patient développe une HTAP et d'autres pas.
Le traitement chirurgical est le traitement de choix dans cette pathologie curable. Les résultats opératoires sont des plus satisfaisants(5). Ces patients retrouvent un cœur quasi sain.

CONCLUSION

Le retour veineux pulmonaire anormal total est la pathologie du nouveau-né et du nourrisson. Elle se manifeste par un tableau d'insuffisance cardiaque. Le diagnostic est fait par échographie cardiaque, l'apport de l'angio-scanner est indéniable. Certains patients peuvent survivre exceptionnellement sans correction chirurgicale comme notre patient de 6 ans. Chez ce dernier, le tableau clinique a mimé une communication inter-auriculaire large.

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Thrombose cardiaque révélant une maladie de Behcet. A propos d'un cas

Behcet disease revealed by a cardiac thrombosis. About one case.

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Résumé

La maladie de Behçet est une vascularite systémique des pays méditerranéens avec un tableau clinique polymorphe associant une aphtose bipolaire, des lésions cutanées, oculaires, articulaires,neurologiques, gastro-intestinales, vasculaires et pulmonaires. Les manifestationscardiovasculaires, en l'occurrence, ont été rapportées, avec atteintes péricardiques, myocardiques, valvulaires, coronariennes et du tissu de conduction, mais elles sont sont rares. La formation intracardiaque du thrombus est exceptionnelle. Nous rapportons le cas d'un patient âgé de 30 ans sans antécédents pathologiques notables qui consulte pour une fièvre prolongée évoluant depuis 2 mois avec altération de l'état général. L'examen physique n'a pas révélé d'anomalies. Le bilan biologique a révélé un syndrome inflammatoire biologique. La sérologie de la Brucellose était négative. L'évolution hospitalière a été marquée par la survenue d'une embolie pulmonaire massive bilatérale avec multiples thrombi flottants des cavités cardiaques droites et un index d'obstruction vasculaire à 55%. Le bilan étiologique de cette embolie pulmonaire n'a pas révélé d'anomalies de la coagulation. Le dosage des marqueurs immunologiques du lupus érythémateux systémique était sans anomalies. L'échocardiographie transthoracique (ETT) a révélé la présence de deux structures hyper-échogènes ovalaires intra-cavitaires cardiaques droites, sur le versant latéral de l'oreillette droite mesurant 30 * 14.6 mmet sur le versant septal du ventricule droit mesurant 11.7 *8.5 mm. Ces structures n'ont pas entrainé de dilatation des cavités cardiaques droites ni d'hypertension artérielle pulmonaire L'échocardiographie transoesophagienne (ETO) a révélé deux masses hyper-échogènes appendues au toit de l'oreillette droite mesurant respectivement 21.5*12.5 mm et 20.6*15 mm (figure 3) et a confirmé la masse intra-ventriculaire droite.La prise en charge thérapeutique a consisté en un traitement médical exclusif associant des anti-vitamines K des corticoïdes et des immunosuppresseurs. L'évolution a été marquée par une amélioration clinique et échocardiographique.

Mots-clés

Maladie de Behcet/ Thrombose cardiaque/ Embolie pulmonaire/ Echocardiographie

Summary

Behcet disease is a systemic vasculitis widespread in Mediterranean countries. It is a multisystem disease characterized by oro-genital ulceration, skin, articular, neurological, gastrointestinal , vascular and lung lesions . The cardiac symptoms such pericardial, myocardial, valvular, coronary or conductive manifestations seem to be rare. Cardiac thrombosis is exceptional.

We present the case of a 30 year-aged patient, with no medical history, who had prolonged fever since two months. Physical examination revealed no abnormalities. Laboratory tests revealed an inflammatory syndrome. Brucellosis serology was negative. During his hospital-stay, he developed a bilateral massive pulmonary embolism with multiple floating thrombus of the right heart and a vascular obstruction index at 55 %. The etiologic diagnosis did not reveal any abnormalities of coagulation and the immunological markers of systemic lupus erythematosus were normal. The transthoracic echocardiography (TTE) showed the presence of two rounded masses of high echogenicity : a 30 * 14.6 oval mass in the lateral wall of the right atrium and a 11.7 * 8.5 mm mass in the septal side of the right ventricle. These masses did not lead neither to the dilatation of the right heart chambers nor to pulmonary hypertension. The transoesophagal echocardiography (TEE) showed the two masses appended to roof of the right atrium respectively measuring 21.5 * 12.5 mm and 20.6 *15 mm. Therapeutic management was entirely medical with vitamin K antagonist, corticosteroids and immunosuppressive drugs. The outcome was marked by clinical and echocardiographic improvements.

Keywords

Behcet disease/ Cardiac thrombosis/ pulmonary embolism/ Echocardiography

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INTRODUCTION

La maladie de Behçet est une vascularite systémique qui affecte principalement de jeunes adultes dans les pays méditerranéens, du Moyen-Orient et d'Extrême-Orient. Le diagnostic est très difficile en l'absence de test diagnostique.
Le tableau clinique est polymorphe associant une aphtose bipolaire, des lésions cutanées, oculaires, articulaires, neurologiques, gastro-intestinales, vasculaires et pulmonaires.
Les manifestations cardiovasculaires, en l'occurrence, ont été rapportées, avec atteintes péricardiques, myocardiques, valvulaires, coronariennes et du tissu conductif,mais sont rares. La formation intracardiaque du thrombus est exceptionnelle.

CAS CLINIQUE

Il s'agit d'un patient âgé de 30 ans originaire de la région de Kairouan sans antécédents pathologiques notables qui consulte pour une fièvre prolongée chiffrée entre 38°C et 39°C évoluant depuis 2 mois.
- L'interrogatoire retrouve une altération de l'état général concomitante à l'apparition de la fièvre avec asthénie, anorexie, amaigrissement et apparition d'une toux sèche.
- L'examen physique n'a pas révélé d'anomalies cliniques.
- L'électrocardiogramme a montré une tachycardie sinusale à 100 battements par minute.
- La radiographie du thorax n'a pas montré d'anomalies.
- Le bilan biologique a révélé un syndrome inflammatoire biologique avec un taux de C-Réactive Protein à 198 mg/l et une vitesse de sédimentation (VS) à 147 secondes à la première heure. La numération de la formule sanguine (NFS) a révélé une hyperleucocytose à 16 800 éléments/mm3 à prédominance de polynucléaires neutrophiles (83% de PNN). La sérologie de la Brucellose était négative.
- L'évolution hospitalière a été marquée par la survenue rapide de douleurs basi-thoraciques droites et de dyspnée. La radiographie du thorax a montré une opacité périphérique du 1/3 moyen du champ pulmonaire droit. La tomodensitométrie thoracique a permis le diagnostic d'embolie pulmonaire massive bilatérale avec multiples thrombi flottants des cavités droites et un index d'obstruction vasculaire à 55%.
- Le bilan étiologique de cette embolie pulmonaire n'a pas révélé d'anomalies, notamment le dosage des Protéines C et S, du facteur V de Leiden, l'antithrombine III. Le dosage des marqueurs immunologiques du lupus érythémateux systémique était sans anomalies, notamment les anticorps anti-phopholipides, les anticorps anti-nucléaires, les anticorps anti-cardiolipines, les anticorps anticoagulants circulants, les anticorps anti B2GP1.
- L'échocardiographie transthoracique (ETT) a révélé la présence de deux structures hyper-échogènes ovalaires intra-cavitaires cardiaques droites, sur le versant latéral de l'oreillette droite mesurant 30 * 14.6 mm (Figure 1) et sur le versant septal du ventricule droit mesurant 11.7 *8.5 mm (Figure 2).

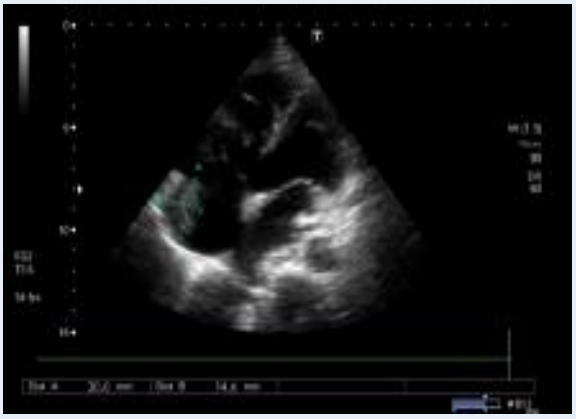

Figure 1 : Masse intra-auriculaire droite à l'échocardiographie transthoracique

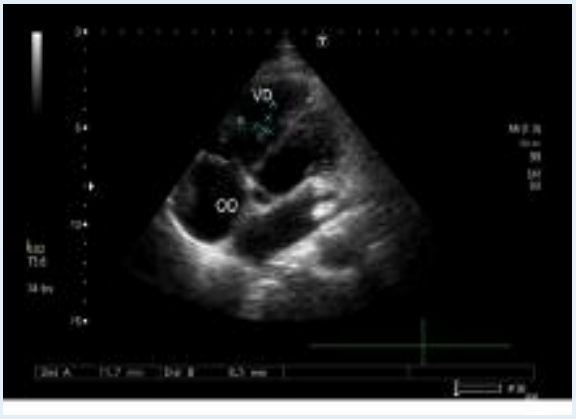

Figure 2 : Masse intra-ventriculaire droite à l'échocardiographie transthoracique.

Ces structures n'ont pas entrainé de dilatation des cavités cardiaques droites ni d'hypertension artérielle pulmonaire (Tableau 1). L'échocardiographie transoesophagienne (ETO) a révélé deux masses hyper-échogènes appendues au toit de l'oreillette droite mesurant respectivement 21.5*12.5 mm et 20.6*15 mm (figure 3) et a confirmé la masse intra-ventriculaire droite.

Tableau 1 : Principales données echocardiographiques

Structure	Valeur
Septum inter-ventriculaire	10.3 mm
Diamètre du VG DTD	47.9 mm
Paroi postérieure du VG	10.3 mm
Fraction d'éjection	53.1%
Diamètre du VD DTD	24.5 mm
PAPS	27 mm Hg

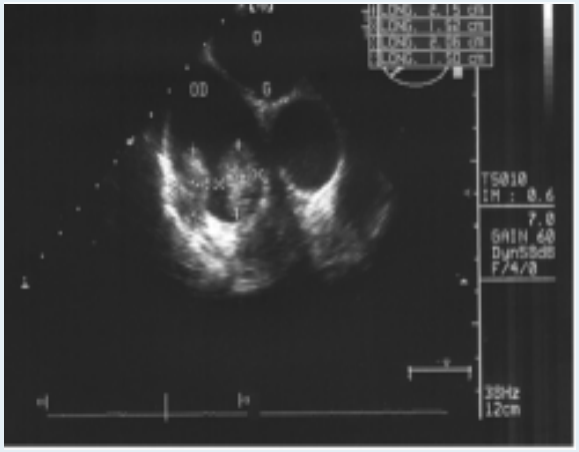

Figure 3 : Masse intra-auriculaire droite à l'échocardiographie transoesophagienne.

- La prise en charge thérapeutique faisait appel à un traitement médical exclusif associant des anti-vitamines K, des corticoïdes et des immunosuppresseurs selon le schéma suivant :
- Acénocoumarol 3mg/jour
- Prednisone 1mg/Kg/j
- Cyclophosphamide 0.6 g/m² en 3 bolus à 1 mois d'intervalle.
- L'évolution a été marquée par une amélioration clinique et échocardiographique.
- Le patient a bénéficié d'un suivi régulier mensuel pendant 9 mois. Il était asymptomatique. L'échocardiographie transthoracique de contrôle à 6 mois de suivi a noté une régression des thrombi intra-cardiaques avec persistance d'une seule image hyperéchogène faisant 9 mm de grand axe sur le versant latéral de l'oreillette droite.

DISCUSSION

La prévalence de la localisation cardiaque et vasculaire de la maladie de Behcet est sous-estimée. Une étude autoptique systématique de la Lakhaupal et Al [1] a retrouvé ce type de localisation dans 16.5% des cas. Les atteintes les plus fréquemment observées sont la cardiomyopathie, la fibrose endomyocardique, la myocardite, la péricardite, l'endocardite, la dysfonction valvulaire, les troubles de conduction par atteinte du tissu conductif, l'atteinte coronaire avec cardiopathie ischémique, les pseudo-anévrysmes artériels, la rupture du sinus de Valsalva et les thromboses intra-cardiaques [2, 3, 4, 5]. La majorité des thromboses cardiaques touchent électivement les cavités droites. Elle intéresse plus fréquemment les ventricules que les oreillettes [6]. La fréquence de l'atteinte vasculaire est très variable selon les séries [7-13] allantes de 6 à 38 % avec une prévalence plus importante dans le pourtour méditerranéen. En Tunisie, la prévalence de la thrombose veineuse profonde (TVP) varie entre 24.9% et 43% [14, 15,16]. Dans notre cas, nous n'avons pas noté d'atteinte vasculaire, l'embolie pulmonaire étant secondaire aux thrombi intracardiaque droit et non pas à une atteinte propre vasculaire pulmonaire.

Le mécanisme éthiopathogénique des thromboses cardiaquesdans la maladie de Behcet reste inconnu. L'examen anatomopathologique des fragments de biopsie myocardique note un tissu fibreux dense, avec des néo-vaisseaux, une inflammation de l'endocarde à des degrés variables avec un infiltrat de cellules mononucléaires, de granulocytes et de polynucléaires neutrophiles [17]. Il existe une association fréquente entre thrombose cardiaque et fibrose endomyocardique [1, 17,18 ,19], ceci pouvant être en rapport avec des séquelles d'endocardite et/ou de myocardite.Dans notre cas, le patient n'a pas bénéficié d'une biopsie endomyocardique à cause du risque élevé de complications et de lanon contribution de la biopsie à la décision thérapeutique.

Le syndrome inflammatoire biologique confirme l'implication d'un processus inflammatoire dans la genèse de cette pathologie avec une vitesse de sédimentation accélérée et un taux sérique de C-ReactiveProtein (CRP) élevé, comme cela a été retrouvé chez notre patient.

De nombreuses anomalies constitutionnelles de l'hémostase ont été retrouvés au cours de la thrombose cardiaque de la maladie de Behcet : déficit en protéine C, déficit en protéine S, mutation du gène de la prothrombine ou homozygotie pour le facteur V de Leiden, anticorps anti-phospholipides (APL), facteur de Von Willbrand. Les anticorps anti-¤ Enolase sont des anticorps spécifiques de la maladie de Behcet dirigés contre cette protéine cible à la surface des cellules endothéliales [19-23]. L'association d'une élévation modérée de l'homocystéine plasmatique avec une atteinte vasculaire et ophtalmique a été rapportée dans la littérature, ce taux étant supérieur à la moyenne de la population générale indemne de la maladie [24-29]. Dans notre cas le dosage des facteurs de coagulation (Protéines C et S, du facteur V de Leiden, l'antithrombine III) n'a pas révélé d'anomalies.

Concernant le tableau clinique, l'hémoptysie est le symptôme révélateur le plus fréquent. Elle est secondaire soit à un anévrysme soit à une artérite des artères pulmonaires [16,30]. Une insuffisance cardiaque au décours d'une fibrose endomyocardique peut être un symptôme révélateur. Une échocardiographie de routine peut être une fréquente circonstance de découverte [31, 32,33]. Dans notre cas les symptômes révélateurs ont été une fièvre prolongée et une dyspnée d'apparition secondaire révélant ainsi une embolie pulmonaire.

La majorité des thromboses cardiaques touchent électivement les cavités droites. Elle intéresse plus fréquemment les ventricules que les oreillettes [34]. Le diagnostic différentiel échocardiographique est un myxome ou une tumeur intra-cardiaque [15, 19,34,35]. Le diagnostic de thrombus cardiaque peut être confirmé par l'IRM cardiaque ou la scintigraphie aux plaquettes marquées à l'Indium111 [36]. Chez notre patient, l'échocardiographie transthoracique et trans-oesophagienne ont suffi pour établir le diagnostic d'une double thrombose intra-auriculaire droite et intra-ventriculaire droite.

Concernant le traitement, il n'y a aucun consensus ou recommandation concernant les thromboses cardiaques. La résolution du thrombus sous traitement médical est possible. Le traitement est à base de corticoïdes, seuls ou en association avec la colchicine et/ou immunosuppresseurs (ciclosporine, azathioprine, cyclophosphamide). Le traitement médical devrait être maximal d'emblée dans les formes graves tels que les anévrysmes artériels et les embolies pulmonaires. L'usage des anti-Vitamine K et de l'aspirine devrait tenir compte du risque hémorragique, surtout en cas d'hémoptysie associées [15,19, 37]. Dans certains cas avec atteinte des artères pulmonaires, l'amélioration a été plus nette avec le traitement immunosuppresseur par rapport aux traitements anticoagulants [38,39,40]. Certaines équipes recommandent le recours systématique à la chirurgie cardiaque comme traitement de première intention des thromboses cardiaques au cours de la maladie de Behcet, mais cette approche reste grevée d'un taux de mortalité élevé [41, 42]. Dans notre cas, la prise en charge thérapeutique faisait appel à un traitement médical exclusif associant des anti-vitamines K des corticoïdes et des immunosuppresseurs avec amélioration nette et régression des thrombi. Nous n'avons pas eu recours à la chirurgie.

La localisation cardiaque de la maladie de Behcet est en général associée à un pronostic réservé avec une mortalité de 20% dans les mois à années faisant suite au diagnostic [43]. Les étiologies les plus importantes de ce pronostic réservé sont les hémoptysies foudroyantes, les embolies pulmonaires, la rupture aortique ou l'infection.

CONCLUSION

Les thromboses intracardiaques sont reconnues comme unecomplication classique de la maladie de Behcet [44]. La découverte d'une masse intra-cardiaque chez un sujet jeune doit faire évoquer le diagnostic de maladie de Bechet, même en l'absence de facteur ethnique ou géographique prédisposant. Ces thromboses sont extrêmement rares, touchent essentiellement le cœur droit et peuvent se compliquer d'embolies pulmonaires. Elles sont fréquemment associées à d'autres thromboses veineuses, notamment de la veine cave supérieure au syndrome des APL. Le développement d'une fibrose endomyocardique joue probablement un rôle majeur dans la genèse de ces thromboses, en témoigne la régression rapportée dans quelques cas de ces thromboses uniquement sous traitement corticoïde et immunosuppresseur sans anticoagulants [44,45].

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