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**SESSION PARALLÈLES « RECHERCHE »**

- **CARDIOMYOPATHIES**

DAGRENAT Charlotte

## DILATED CARDIOMYOPATHY AND PHENOTYPE – GENOTYPE CORRELATIONS: ABOUT A COHORT OF PATIENTS WITH FILAMIN C GENE MUTATION

***Background*** : *FLNC* truncating variants are correlated with cases of dilated cardiomyopathy (DCM) characterized by a potentially severe rhythmic phenotype with a high incidence of sudden cardiac death.

***Objective*** : The objective of this study was to determine whether there is a specific clinical and MRI profile associated with *FLNC* gene mutations in patients with DCM. We hypothesize that there is a particular profile of cardiac fibrosis with CMD associated to *FLNC* mutation.

***Methods*** : This was a retrospective, multicenter, observational study conducted at the Centre Hospitalier Universitaire de la Pitié Salpêtrière and the Hôpitaux Universitaires of Strasbourg, France. Index - patients with impaired left ventricular ejection fraction (LVEF) with or without left ventricular dilatation associated with a *FLNC* gene mutation were included in the study. Related cases carrying the mutation were also included.

***Results*** : A cohort of 24 patients from 14 families was analyzed for this study. There was at least one sudden cardiac death in 9 families (64.3%), and at least one myocarditis in 3 families (21.4%). Among the 24 patients, 19 cardiac magnetic resonance imaging were analyzed, including 9 performed in index cases and 10 in relatives. More than 2/3 of the patients had systolic left ventricular dysfunction with a mean LVEF of 42.1%. The LGE was observed in nearly ¾ of patients (73.7%) and precedes systolic dysfunction in 21.4% of patients. This LGE was mostly diffuse and extensive with an average of 6 ± 5.9 affected segments (out of 17) and a majority of subepicardial layout ($p<0.02$), preferentially the infero-latero-basal (83.3%), infero-basal (75%), and infero-medial (75%) segments.

***Conclusion*** : This study shows a particular profile associated with *FLNC* gene mutations in patients with DCM with a characteristic distribution of LGE, predominantly subepicardial in half of the cases, concentric, sparing the apex and associated with an increased risk of ventricular rhythm disorders, with nearly two thirds of the families affected by sudden death and one fifth of the families with myocarditis.

DAGRENAT Charlotte

## CARDIOMYOPATHIE DILATEE ET RELATIONS PHENOTYPE – GENOTYPE : A PROPOS D'UNE COHORTE DE PATIENTS AVEC MUTATION DU GENE DE LA FILAMINE C

***Introduction*** : Les variants tronquants de *FLNC* sont corrélés à des cas de cardiomyopathies dilatées (CMD) caractérisés par un phénotype rythmique potentiellement sévère avec un taux d'incidence de mort subite élevé.

***Objectif*** : L'objectif de cette étude était de déterminer s'il existe un profil clinique et IRM particulier associé aux mutations du gène *FLNC* chez les patients avec CMD. L'hypothèse principale de cette étude était qu'il existe un profil particulier de fibrose myocardique dans les CMD associées à une mutation du gène *FLNC*.

***Matériel et méthodes*** : Il s'agit d'une étude observationnelle, rétrospective et multicentrique, menée au Centre Hospitalier Universitaire de la Pitié Salpêtrière et aux Hôpitaux universitaires de Strasbourg. Les patients cas-index présentant une altération de la fraction d'éjection du ventricule gauche avec ou sans une dilatation ventriculaire gauche associée à une mutation du gène *FLNC* étaient inclus dans l'étude. Les cas apparentés porteurs de la mutation étaient également inclus. Les critères d'exclusion étaient : les cardiomyopathies hypertrophiques, les variants non pathogènes et les variants de signification indéterminée (VSI).

***Résultats*** : Une cohorte de 24 patients issue de 14 familles a été analysée. On relève au moins une mort subite dans 9 familles (64.3%), et au moins une myocardite dans 3 familles (21.4%). Parmi les 24 patients, 19 imageries par résonance magnétiques cardiaques ont pu être analysées dont 9 réalisées chez des cas index et 10 chez des cas apparentés. Plus de 2/3 des patients présentent une dysfonction ventriculaire gauche systolique avec une FEVG moyenne à 42.1%. Le rehaussement tardif (RT) est objectivé chez 73.7% des patients et précède la dysfonction systolique chez 21.4% des patients. Ce RT est principalement diffus et étendu avec en moyenne 6 ± 5.9 segments touchés (sur 17), une majorité de localisation sous épicardique ($p<0.02$), préférentiellement les segments inféro-latéro-basal (83.3%), inféro-basal (75%), et inféro-médial (75%).

***Conclusion*** : Cette étude objective un profil particulier associé aux mutations du gène *FLNC* chez les patients avec CMD avec une distribution du RT caractéristique à prédominance sous-épicardique dans la moitié des cas, concentrique épargnant l'apex et associé à un risque de troubles du rythme ventriculaires accru, avec près de 2/3 des familles affectées par des morts subites et 1/5$^{e}$ des familles avec myocardites.

## DE LA VILLEON Grégoire

**Impact of a transition education program on health-related quality of life in adolescents and young adults with congenital heart disease**

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**BACKGROUND AND AIM:** Recent advances in the field of congenital heart disease (CHD) led to an improved prognosis of the patients and in consequence the growth of a new population: the grown up with congenital heart disease. Until recently, more than 50% of these patients were lost to follow up because of the lack of specialized structures. The critical moment is the transition between paediatric and adult unit. Therapeutic education is crucial to solve this issue by helping patients to become independent and responsible. The
TRANSITION randomized trial aims to assess the impact of a transition education program on health-related quality of life (HRQoL) of adolescents and young adults with CHD.
**METHODS:** Multicentre, randomised, controlled, parallel arm study in patients with CHD aged from 13 to 25 years old. Patients were randomised into 2 groups (transition education program vs. no intervention). The primary outcome was the change in self-reported HRQoL (PedsQL generic questionnaire) between baseline and 12-month follow-up. Using an intention-to-treat analysis, a total of 200 patients were required to observe a significant increase of the overall self-reported HRQoL score (80% power, 5% α-risk). The secondary outcomes were proxy-reported HRQoL scores, clinical outcomes, cardiopulmonary exercise test parameters (VO2max, VE/VCO2 slope, anaerobic threshold, oxygen pulse), the level of physical activity, the level of knowledge of the disease using the Leuven knowledge questionnaire for CHD, physical status and psychological status.
Trial registration: NCT03005626. Study design, DOI: 10.1186/s12955-021-01668-1. **RESULTS:** A total of 189 patients were enrolled in the trial (mean age 18.6±3.6 years, sex ratio=1). We observed a significant difference of 3.9±1.1 points (P=0.04) in the primary outcome, i.e., the self-reported PedsQL total score, in favour of the transition education group. Significant differences were also observed in the self-reported PedsQL psychosocial score (4.2±1.2 points, P=0.049), the proxy-reported physical score (6±2.3 points, P=0.01), and the disease knowledge score (4.9±0.7 points, P<0.001). No significant group differences were observed in the clinical or CPET parameters.
**CONCLUSIONS:** The HRQoL of adolescents and young adults with CHD was improved by our transition education program. The supervision of the program by a specialist nurse as“transition care manager” is probably an interesting operating model to follow.

**Keywords:** transition; therapeutic education; congenital heart disease; quality of life; adolescent.

FONTANGES Pierre-Alexandre

**Clinical Hypnosis associated with local anesthesia for cardiac catheterization in paediatric population**

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Hypnosis is a promising non-pharmacologic adjunct treatment for improving pain and interventional anxiety management in paediatric interventions. Its efficiency and impacts in paediatric cardiac catheterization (CC) are unknown.

**Methods**: In a prospective monocentric study, all patients aged <18 years who had CC under hypnosis with local anesthesia from January to December 2021 were included. Pain and anxiety were evaluated by the ANI (Analgesia Nociception Index) measured during the intervention, and the Visual Analogue Scale (VAS) assessed by the patients after the intervention.

**Results:**
Sixteen patients were included. Median age was 10.5 years old |range 4-16 years], Median weight was 37 kg [range 15-79 Kg]. Catheterizations were interventional in 10 patients (62.5%) and for diagnostic purposes in 6 patients (37.5%) (table1). Hypnosis indications were general anesthesia (GA) contraindication in 4 patients (25.0%), the need of accurate pressures measurements without GA interference in 2 patients (12.5%) and interventionist/patients preferences in 10 patients (62.5%). In one patient of 4 years old, the hypnotic status was not achieved and the procedure was aborted before the installation. Procedures were accomplished successfully in 15 patients (93.7%) without any additional sedation even in challenging cases; large atrial septal defect (ASD) closed with 39 mm Occlutech device in 16 years old patient, and catheterization in 14 years old patient with Fontan failure, elevated pulmonary vascular resistances, cyanosis (Hemodynamic Vulnerability Score=5) with GA contraindication. Median procedures and fluoroscopy times were 67.5 min and 5.3 min respectively. In one case, pulmonary artery pressures normalized comparing to previous catheterization under local anesthesia alone leading to the cancellation of cardiac surgery on mitral stenosis. VAS score was under 5/10 in all patients. The ANI remained above 50 (non painful zone) in all but one patient. No significative decrease of the ANI was found during the intervention comparing to baseline (p=0.62). One patient with language difficulties had short and transient decrease of the ANI (49) during one minute after the puncture. No complications were recorded.

**Conclusion:** Paediatric CC are feasible under hypnosis even in complicated cases. Hypnosis was efficient to manage pain and stress in all cases, it ensures more reliable pressures measurements.

## PALMYRE Aurélien

**Comparison of targeted genetic testing versus next generation sequencing of panels for the diagnosis of Fabry Disease or Transthyretin Amyloidosis in patients with hypertrophic cardiomyopathy**

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Abstract

**Introduction and objective**. The appropriate identification of the causes of hypertrophic cardiomyopathy (HCM), or left ventricular hypertrophy (LVH), is especially crucial for rare causes with existing specific therapies, such as Fabry disease or transthyretin amyloidosis (ATTR). Two alternative sequencing strategies are used: targeted Sanger sequencing of *GLA* and *TTR* genes or NGS-based multi-gene panels sequencing, according to clinical context. We aimed to identify the most efficient strategy for Fabry or ATTR amyloidosis diagnosis.

**Methods**. We studied 342 index patients with LVH/HCM with or without a suspicion of ATTR or Fabry disease. Patients were subjected either to a NGS-based strategy through a panel of 107 genes involved in cardiomyopathies, or to a Sanger sequencing-based strategy, targeted to *TTR* or *GLA* gene in case of a suspicion of amyloidosis or Fabry disease. Then, we calculated the time required for each analysis as the days elapsed between the date of specimen reception in the laboratory and the date of result validation in the final analysis report. Finally, we fixed the cost of each analysis to their respective French prices (RIHN nomenclature).

**Results**. A total of 299 patients was analysed through NGS approach (40,8±18,2 years old, LVH 19.7±5.0 mm), 29 patients via Sanger sequencing of *TTR* (65.1±18.1 years old, LVH 17.4±4.0 mm) and 13 via Sanger sequencing of *GLA* (49.5±16.2 years old, LVH 17.9±4.3 mm). We observed that the yield of pathogenic variant identification (class 5 or 4) was more important with the targeted Sanger strategy (in case of ATTR or Fabry suspicion) than with the NGS/panel strategy (11/42=26.2% vs. 4/299=1.3%; p value<0.01). The delay for genetic results was significantly shorter when applying the targeted Sanger strategy versus the NGS-based approach (26±90 days vs 193.5±36.7 days, p value<0.01). Costs were 1503.90€ for NGS-based, 615.60€ for *TTR* Sanger, 769.50€ for *GLA* Sanger.

**Conclusion**. Both strategies are useful for the identification of these rare causes. However, targeted Sanger sequencing is more efficient, faster and less expensive than NGS technology. Hence, systematic search of red flags raising the suspicion of ATTR or Fabry disease appears crucial for selecting the optimal strategy and reduce the delay of diagnosis and improve the care of patients with LVH/HCM.

PIRIOU Nicolas

**Analyse du phénotype des cardiomyopathies arythmogènes**

**à prédominance ventriculaire gauche par échocardiographie de déformation**

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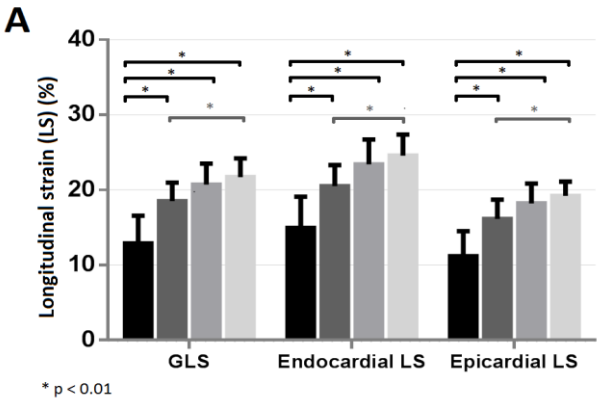
**Introduction :** Les cardiomyopathies arythmogènes (CA) sont caractérisées par une dégénérescence myocardique fibro-adipeuse. Certains phénotypes de CA se présentent avec une atteinte du ventricule gauche (VG) isolée ou prédominante (CAVG). La caractérisation d'une fibrose sous-épicardique par IRM est le seul critère morphologique majeur pour le diagnostic des CAVG. Il peut parfois s'agir de la seule anomalie phénotypique, sans anomalie de la cinétique segmentaire ou de la fonction VG globale détectable en échocardiographie transthoracique (ETT).




**Objectif :** Décrire le phénotype échocardiographique des CAVG en utilisant les données ETT incluant le 2D-strain, avec une analyse du strain longitudinal global (SLG) et multicouches au niveau biventriculaire.

**Méthode et résultats :** Nous avons analysé en ETT standard et de déformation 57 patients avec variant pathogène sur des gènes impliqués dans les CAVG et 28 apparentés sans variant pathogène. Parmi les patients porteurs d'un variant pathogène, l'IRM cardiaque distinguait des patients avec phénotype complet de CAVG ($n$ = 25), fibrose VG isolée ($n$ = 17), absence de phénotype de CAVG ($n$ = 15). Ces patients présentaient des paramètres ventriculaires droits (VD) préservés et un échappement aux critères classiques de CAVD. Le rehaussement tardif IRM prédominait en région sous-épicardique, notamment en territoire inférieur et latéral. En ETT, les patients avec phénotype complet de CAVG et fibrose VG isolée présentaient des paramètres de strain altérés par rapport aux apparentés sains sans variant pathogène, avec une atteinte prédominante du strain longitudinal sous-épicardique (Figure A). Les paramètres du strain des patients porteurs de variant pathogène sans phénotype de CAVG et sans fibrose VG isolée n'étaient pas différents de ceux des apparentés sains sans variant pathogène.

**Conclusion :** Le diagnostic de CAVG nécessite la réalisation d'une IRM cardiaque mais l'ETT représente la première modalité d'évaluation des cardiomyopathies. L'analyse des différents paramètres issus du 2D-strain semble permettre d'améliorer la sensibilité de l'ETT pour le diagnostic de CAVG, particulièrement en cas de fibrose VG isolée.

## CHARRON Philippe -PROUKHNITZY Julie

**Analyse des complications cardiovasculaires de la maladie de Fabry dans une large cohorte française.**

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Introduction
La maladie de Fabry est une maladie lysosomale liée à l'X dont la principale cause de mortalité est désormais cardiovasculaire. L'histoire des complications cardiovasculaires majeures (MACE) et ses déterminants sont mal connus.

Objectifs :
L'objectif de cette étude est de décrire les MACE de la maladie de Fabry et de préciser les facteurs associés à leur survenue.

Méthodes.
Cette étude rétrospective porte sur les patients avec maladie de Fabry inclus dans la cohorte FFabry (registre français multicentrique de médecine interne) et dans le Centre de référence des maladies cardiaques héréditaires du CHU Pitié Salpêtrière. Les MACE sont définies par la survenue de troubles conductifs de haut degré, de TV ou FV, d'arythmies atriale, l'implantation d'un PM ou DAI, la survenue d'insuffisance cardiaque sévère (IC) ou terminale, de myocardite ou d'infarctus du myocarde. Le lien entre ces MACE et le sexe, et l'âge au diagnostic et le phénotype classique ou non classique de maladie de Fabry a été analysé.
Résultats.
131 patients adultes ont été inclus, 21% des patients ont présenté des MACE (IC 23%, 19% TSV), à un âge médian de 42 ans. Le taux de MACE n'était pas statistiquement différent selon le sexe mais survenait plus précocement. Les patients atteints de MACE avaient un âge au diagnostic de la maladie plus tardif ($p<0.01$). Les hommes avec un phénotype classique présentaient MACE plus précocement que les femmes et le phénotype non classique ($p <0.0001$).
Conclusion.
Cette étude porte sur la plus grande cohorte française de maladie de Fabry. Le taux de complications cardiovasculaires est important et touche également les deux sexes, plus précocement chez les hommes. Le taux de complication est significativement associé à un âge plus tardif au diagnostic de maladie de Fabry et significativement associé au phénotype classique suggérant un effet très défavorable du retard au diagnostic. Il paraît important d'améliorer le diagnostic de maladie de Fabry, de mieux prendre en charge les patients avec phénotype classique ainsi que les femmes avec maladie de Fabry.

## RÉANT Patricia

**Caractérisation de la fonction veineuse et endothéliale dans la cardiomyopathie hypertrophique symptomatique : étude pilote HCM-Vein**

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**Introduction :** L'obstruction dans la cardiomyopathie hypertrophique (CMH) est un phénomène dynamique complexe, potentiellement influencé par différents facteurs incluant les conditions de charge et donc le retour veineux. La CMH peut également être associée à une dysfonction endothéliale et microvasculaire périphérique. Nous suspectons qu'un faible volume de recrutement du réseau veineux et la dysfonction endothéliale vasculaire pourraient être le reflet d'une atteinte globale et plus sévère de cette maladie.
**Objectif** : L'objectif principal était d'étudier le degré d'insuffisance veineuse et de dysfonction endothéliale chez des patients porteurs de CMH obstructive (CMHO) symptomatique comparativement à des sujets sains.
**Matériels et méthodes** : Etude monocentrique, prospective, pilote, comparant les paramètres d'évaluation de la fonction veineuse par pléthysmographie veineuse et de la fonction endothéliale (étude en Doppler artériel de la Flow Mediated Dilatation (FMD) et analyses de biomarqueurs sériques) chez des patients avec CMH obstructive et des sujets contrôle sains.
**Résultats** : Parmi les 30 patients avec CMHO symptomatiques, 30% (n=9) présentaient une fraction de volume résiduel veineux (FVRv) anormale témoignant d'une pression veineuse ambulatoire élevée *vs.* 0% chez les 10 sujets contrôles sains.

En comparant les patients CMHO avec FVRv anormale (n=9) aux autres patients CMHO avec FVRv normale (n=21), il n'y avait pas de différences en termes d'âge, de sexe (67% d'hommes), et sur les paramètres échocardiographiques classiques au repos comme à l'effort. Il n'y avait pas de différence significative en termes de FMD non plus entre les 2 groupes mais 56% des patients CMHO avec FVRv anormale avaient une élévation du facteur de Willebrand (*vs.* 26% des autres patients CMHO), 33% avaient un index de remplissage veineux anormal (*vs.* 10%) et 78% avaient une fraction d'éjection veineuse anormale (*vs.* 57%).

**Conclusion** : Il existe une insuffisance veineuse chez environ 30% des patients avec CMHO symptomatique dans cette étude pilote. Cela mérite d'être confirmé par une étude plus large qui intégrera l'impact sur la sévérité, et donc le pronostic, de cette maladie.

- **TROUBLES DU RYTHME**

## ARNAUD Marine

**Characteristics and prognosis of the Catecholamine induced QT prolongation syndrome**

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Background: We have recently demonstrated association of unexplained sudden cardiac arrest (SCA) with inheritance of catecholamine induced QT prolongation (CIQTP).

Objective: We here aim to describe incidence, characteristics, and prognosis of this new syndrome in young patients with unexplained SCA or their relatives.

Methods: We reviewed the medical screening of all consecutive patients, or their first-degree relatives explore from 2015 after the occurrence of a SCA before age 45. Structural heart disease or inherited arrhythmia diseases were excluded. A mental stress test was performed, as previously described, for each family members. All families with a positive mental stress were included in the study. Genetic screening was performed in at least one positive patient per family using targeted sequencing on a panel of 109 genes associated with inherited arrhythmias and cardiomyopathies.

Results: Among 456 patients screened (24 after SCA, 432 for familial screening) of 153 families, we identified 10 families

(6.5%) with a catecholamine induced QT prolongation. No mutation was identified in these families. One hundred and ten patients were screened in CIQTP families. Thirty-four patients (30.9%) presented a CIQTP (mean age 42±20 yo, 64.7% of women). Five (14.7%) patients presented with previous symptoms (including 4 syncope and 1 SCA).
Two patients (5.9%) were implanted with an ICD and eleven (32.3%) were treated with beta blocker therapy mainly because of QT prolongation > 500 ms after mental stress test or previous symptoms.
After a 3.6±1.8 years of follow up, no sudden cardiac death nor syncope occurred on beta blocker therapy except for one patient implanted with an ICD after a SCA. Under beta blocker treatment the patient was asymptomatic for 5 years. After a suddenly stop of the beta blocker treatment, the patient underwent VF. For 3 years now the patient is asymptomatic under beta blocker treatment.

Conclusions: In our experience, CIQTP families represent 6.5% of cases of unexplained SCD and suggest systematic screening with a mental stress test for family screening after the occurrence of a SCA. Beta blocker therapy is very efficient to reduce the risk of SCA.

## BANOS Adeline

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***Après une mort subite récupérée, quel traumatisme pour le patient et ses proches ? TEMPO***

Malgré les avancées thérapeutiques, la mort subite d'origine cardiaque reste une maladie fréquente

(60000/an en France) et souvent mortelle (5 % de survie) (Bougoin W et al. Intensive Care Med 2014). Parce qu'il est par définition inattendu, l'impact psychologique sur les patients réanimés et sur leurs proches peut être important. Cependant, peu d'études l'ont évalué. Les patients qui développent plus tard un trouble de stress post-traumatique (TSPT) présentent généralement un trouble de stress aigu. Chez les patients en mort subite d'origine cardiaque réanimés, une détresse psychologique aiguë est fréquente (Schaff et al, 2012) et un TSPT a été identifié chez 40 % des patients (Zimmerli, 2014). Concernant les proches, Haywood (2018) les appelle les « patients oubliés » pour souligner l'absence de reconnaissance de leur traumatisme

psychologique. Le TSPT était plus fréquent chez les personnes témoins de la mort subite récupérée que chez celles qui n'y étaient pas. Hofland et al (2018) ont montré que les personnes présentes lors des manœuvres de réanimation avaient un stress plus aigu que les autres. Cette étude évaluera l'état de stress aigu avec l'échelle SASRQ chez les patients réanimés d'une mort subite cardiaque et leur proche juste après l'événement. À 3 mois, la présence d'un TSPT sera évaluée avec PCL-5 et LEC-5 chez les patients et leurs proches.
Objectif principal : nombre de patients et de proches atteints d'un TSPT à 3 mois après la réanimation de leur mort subite d'origine cardiaque.
Objectifs secondaires : nombre de patients souffrant d'un trouble de stress aigu, de patients ayant des antécédents de TSPT.
Conception de l'étude : étude prospective descriptive, monocentrique

## HADDAD Christelle

**non-invasive myocardial electrical propagation mapping as a new tool to identify an arrhythmogenic substrate in patients with premature ventricular beats: a pilot study**

Christelle Haddad, MD, Antoine Delinière, MD, Leslie Placide, MD, Gilles Millat, PhD, Alexandre Janin, PharmD, PhD, Philippe Chevalier, MD, PhD

### Introduction

Premature ventricular contractions (PVCs) in young people and athletes are usually benign, but they may mark underlying heart disease and risk of sudden cardiac death. Because PVCs may be the only sign of an early stage arrhythmogenic cardiomyopathy **(**AC**)**, there is a need for accurate non-invasive electrophysiological evaluation of young patients with PVCs.

### Objectives

This study aimed to identify electrophysiological footprint of AC through a non-invasive electrocardiographic imaging (Medtronic CardioInsight® Cardiac Mapping System) in patients presenting with isolated PVCs and presumed healthy heart.

### Materials and methods

Twenty patients were prospectively enrolled into two groups from 2019 to 2021. The first group included patients with AC diagnosed when 2010 Task Force Criteria were met. The second group included patients presenting with PVCs and presumed healthy heart. Mapping was performed during sinus rhythm and from PVCs.

## Results

Right ventricular (RV) activation times were significantly longer in patients suffering from AC (17.8±7.2ms vs 33.4±11ms, p=0.01). Left ventricular and total ventricular activation durations also tended to be longer in AC but did not reach statistical significance. Activation sequence was more heterogeneous among patients in the AC group. The basal septal epicardial breakthrough was the most common pattern (40%) in the second group. Voltage maps identified low-voltage zones affecting mainly the RV free wall in most patients suffering from AC. Analysis of the signal showed epsilon waves from the RV in most patients in the AC group even if this pattern was absent in their 12-lead electrograms (Figure 1).

## Conclusion

These present results suggest that high-density electrocardiographic mapping may detect AC at early stages of the disease in patients with PVCs. Future quantification of the predictive value of 3D ECG may facilitate the follow-up and the treatment of PVCs patients with apparently normal heart.

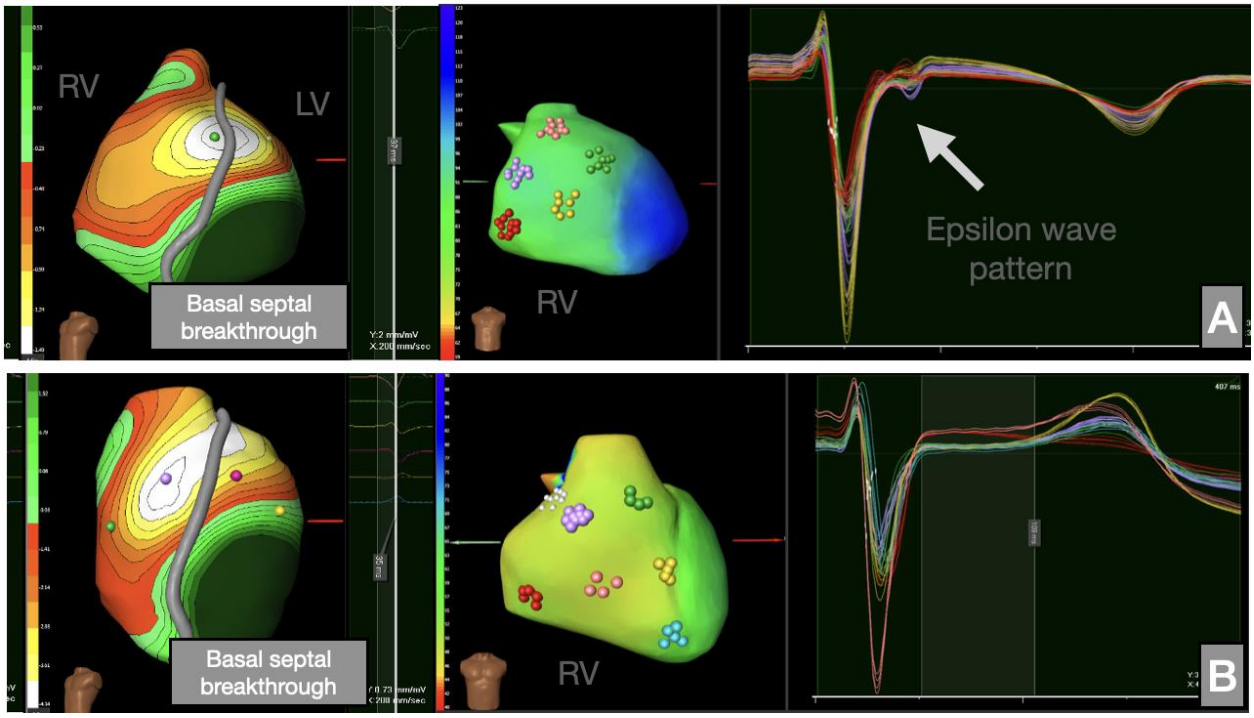


**Figure 1.** Same pattern of activation in two patients from each group **(**A: patient with AC; B: patient with PVCs and presumed healthy heart) associated with electrograms recorded from RV.

## HERMIDA Alexis

**Use of ranolazine as rescue therapy in a patient with Timothy syndrome type 2**

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**Introduction**: Type 2 TS is extremely rare and current knowledge is based on reported clinical cases. We have followed a young patient with the type 2 TS p.(Gly402Ser) mutation for nine years at the Amiens University Hospital.

**Objectives**: During this long-term follow up, the patient has received various treatments combined with very close monitoring, making it possible to obtain highly precise data. We obtained parental permission to report this exceptional case.

**Methods**: We retrospectively collected data about the whole cardiological history of the child.

**Results**: We report a detailed case of type 2 TS due to a p.(Gly402Ser) mutation in exon 8 of the *CACNA1C* gene. The patient shows a marked prolongation of repolarization with a mean QTc of 540 ms. He shows no structural heart disease, syndactyly, or cranio-facial abnormalities. However, he shows developmental delays, without autism, and dental abnormalities. The cardiac phenotype is very severe, with a resuscitated cardiac arrest at 2.5 years of age, followed by 26 appropriate shocks during nine years of follow-up. Adding mexiletine to nadolol resulted in a reduction of the QTc and a slight decrease in the number of appropriate shocks. In early 2020, the occurrence of three appropriate shocks in two months prompted us to replace the mexiletine with ranolazine. We then used therapeutic drug monitoring to find the right dose level. During the 18 months following the switch, the patient did not experience any episodes of ventricular arrhythmia.

**Conclusion**: The present case report is the first to describe the successful treatment of pediatric TS type 2 with ranolazine. Use of the drug has suppressed the need for appropriate shocks for the last 18 months.

## SOUILLA Luc

**Cardiorespiratory fitness in children with Long QT syndrome: a controlled cross-sectional study**

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1) Background

Congenital long QT syndrome (LQTS) is the most frequent inherited arrhythmia, characterized by a prolonged QT interval, and an increased risk of syncope and sudden cardiac death. Because of sports and exercise restrictions, children with LQTS are at risk of physical deconditioning. Guidelines on sports participation in cardiovascular disease have become less restrictive over time, however, the cardiorespiratory fitness has not been well evaluated in the paediatric LQTS population.

2) Aims

We aimed to evaluate, in children with LQTS, the cardiorespiratory fitness, the muscular strength and architecture, and the level of physical activity, in comparison with healthy controls.

3) Methods

This controlled bicentric cross-sectional study enrolled 20 children with LQTS children aged 6 to 17 years old compared to 20 healthy matched subjects. They underwent a complete cardiac check-up with cardiopulmonary exercise test and muscular ultrasound, performed muscle strength by functional tests, and wore a fitness tracker for 14 days (Actigraph GT3X).

4) Results

In children with LQTS, peak oxygen uptake ($VO2_{peak}$) and ventilatory anaerobic threshold were moderately impaired but significantly lower than in healthy controls (33.9±6.2 *vs.* 40.1±6.6 mL/Kg/min, *P=0.004*, d=-0.96; 23.8±5.1, 28.8±5.5 mL/Kg/min, *P=0.005*, d=-0.95, respectively). All children with LQTS had betablockers and a lower maximum heart rate during exercise. LQTS children had lower leg strength (119.5±33.2 *vs.* 147.3±36.1 cm, *P=0.015*, d=-0.8) and muscle pennation angle (12.2±2.4 *vs.* 14.3±2.8°, *P=0.01*, d=-0.8).
There was no difference on moderate-to-vigorous physical activity level between groups (36.67±12.65 min/day *vs.* 41.92±18.29 min/day, *P=0.30*). Overall, 50 % had patterns of muscular deconditioning.

5) Conclusion

Physical capacity in children with LQTS is moderately altered, from multifactorial limitation. Exercise rehabilitation could be of interest in LQTS children with significant physical limitation.

- **CARDIOPATHIES CONGÉNITALES COMPLEXES**

## DESGRANGE Audrey

**Stratification of cardiac malformations in the heterotaxy syndrome based on embryonic mechanisms**

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***Pathologies: Cardiopathies Congénitales Complexes***

Introduction: Left-right asymmetry of cardiac morphogenesis begins with the rightward looping of the embryonic heart tube, which positions cardiac chambers relative to each other to establish the double blood flow. In humans, disturbances in this process have been associated with severe heart defects in the heterotaxy syndrome. We have demonstrated that the left signal Nodal is required in cardiac precursors for shaping the embryonic heart loop (Desgrange et al., 2020). *Nodal* mutants later develop an heterotaxy syndrome with a spectrum of heart defects. However, the heterogeneity of the heterotaxy phenotype has remained poorly understood.
Objectives: We aim to determine the embryonic mechanisms underlying the heterotaxy syndrome. Since *Nodal* mutants at E9.5 display four categories of abnormal heart loops, we reasoned that heterotaxy may be stratified.
Material & Methods: To tackle the challenge of monitoring a specific phenotype at two stages of development in a single embryo, we developed a multimodality imaging pipeline, combining echography, micro-CT and HREM. Phenotyping is based on advanced 3D image analyses and clinical criteria. Correlations between qualitative variables were assessed statistically.
Results: With this unique approach, we have identified heart loop features that are predictive of specific cardiac malformations. For example, in the clinical nomenclature, the final position of the ventricles is considered to reflect the direction of the embryonic heart loop. Our experiments now demonstrate that the clinical and embryonic loops do not correlate, thus indicating that ventricle position is determined after heart looping.
Conclusion: This study provides novel insights into the emergence of complex congenital defects in the heterotaxy syndrome.

## POTTIER India

**Cardiopathies Congénitales Complexes**
**ECMO néonatale en post-opératoire de chirurgie cardiaque : devenir à court et moyen terme**

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*Introduction*

Le traitement des cardiopathies congénitales (CC), quel qu'en soient la nature et le pronostic, est principalement chirurgical et une intervention doit parfois être réalisée dès les premiers jours de vie. L'ECMO (ExtraCorporeal Membrane Oxygenation) est une technique d'assistance circulatoire qui permet de suppléer transitoirement une défaillance hémodynamique engageant le pronostic vital.

*Objectifs*

Étudier la mortalité et le devenir à court et moyen terme des enfants de moins de 60 jours de vie ayant une CC et assistés par ECMO dans les suites d'une intervention de chirurgie cardiaque.

*Matériel et méthodes*

Dans cette étude rétrospective, tous les nouveau-nés de moins de 60 jours opérés d'une CC à l'hôpital Necker puis assistés par ECMO entre le 1er avril 2010 et le 31 mars 2020 ont été inclus.

*Résultats*

Quarante patients ont été inclus avec un âge et un poids médian respectivement de 7 [4 ; 9,7] jours et 3 [2,8 ; 3,2] kg. La survie intra-hospitalière était de 47,5% tandis que la survie globale après une durée médiane de suivi de 3,4 ans était de 35%. Seize enfants (40%) ont présenté une complication neurologique. Vingt-trois enfants (57,5%) ont reçu un traitement anti-infectieux curatif. Tous les patients ont présenté une insuffisance rénale aiguë dont 17 (42,5%) ont nécessité une hémodiafiltration. Après analyse univariée, les CC avec physiologie univentriculaire (p=0,046), celles avec hypertension artérielle pulmonaire (p=0,032) et les complications hémorragiques (p=0,034) étaient significativement associées à la mortalité intra-hospitalière.

*Discussion*

Cette étude est la première à s'intéresser spécifiquement à l'ECMO en post-opératoire de chirurgie cardiaque néonatale. Elle confirme une mortalité et un taux de complications élevés en accord avec la littérature. Le développement de nouvelles techniques d'anticoagulation et de monitorage de l'hémostase, le développement de l'imagerie cérébrale fonctionnelle et la réévaluation des indications d'ECMO peuvent être des pistes d'amélioration des pratiques.

## JALAL Zakaria

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**TITLE:** Ductus arteriosus stenting versus Blalock-Taussig shunt for infants with ductaldependent pulmonary circulation: a comparative multicenter international study.

**INTRODUCTION:** New-borns with congenital heart disease with ductal-dependent pulmonary blood flow (PBF) require an early palliative procedure, either a patent ductus arteriosus stenting (PDAs) or a modified Blalock-Taussig shunt (mBTS).

**AIM:** To compare peri-procedural and mid-term outcomes between PDAs and mBTS through an international multicentre registry.

**METHODS:** Infants<1 month with ductal-dependent PBF palliated with either a PDAs or a mBTS between Jan 2000 and Dec 2019 were reviewed from 10 European participating centres (France n=4, Spain n=5, UK n=1). Peri-procedural and mid-term outcomes were compared between the 2 groups, using a propensity score adjustment.

**RESULTS:** The study cohort was composed of 179 infants who underwent PDAs and 456 infants with mBTS. Median follow-up was 79 months. After propensity score adjustment, no significant differences were found in relation to the primary outcome of survival before next-stage surgery or at 18 months, (mBTS 91.7%, vs PDAs 88%, p=0.69). Patients of PDAs group had a reduced the risk of death before repair compared to mBTS group (hazard ratio, 0.76; [95% CI, 0.55-1.06]; p=0.10). However, the incidence of reintervention before next-stage surgery was more common in PDAs group (28.3% vs

14.1%, p=0.024). In addition, the PDAs group had a lower adjusted intensive care unit length of stay (4 vs 6 days; p<0.001), a lower duration of inotropic support (39 vs 89 hours, p<0.001) and a lower proportion of diuretic use at discharge (39.5% vs 70.7%; p<0.001).
**CONCLUSIONS:** In this large international comparative study, there was no difference in the primary end point between PDAs and mBTS. Although re interventions rate was higher in PDAs group, other markers of perioperative morbidity support PDAs as a reliable strategy.

## FONTANGES Pierre-Alexandre

**Clinical Hypnosis associated with local anesthesia for cardiac catheterization in paediatric population**

*Pierre-Alexandre Fontanges, Julien Haudiquet, Alexandre Delarue, Guillaume Leroy, Olivia Domanski, Nahla Abou Assi, Christian Amenyah, Thameur Rakza, Francois Godart, Jean Benoit Baudelet, Julien De Jonkheere, Ali Houeijeh*

Hypnosis is a promising non-pharmacologic adjunct treatment for improving pain and interventional anxiety management in paediatric interventions. Its efficiency and impacts in paediatric cardiac catheterization (CC) are unknown.

**Methods**: In a prospective monocentric study, all patients aged <18 years who had CC under hypnosis with local anesthesia from January to December 2021 were included. Pain and anxiety were evaluated by the ANI (Analgesia Nociception Index) measured during the intervention, and the Visual Analogue Scale (VAS) assessed by the patients after the intervention.

**Results:**
Sixteen patients were included. Median age was 10.5 years old |range 4-16 years], Median weight was 37 kg [range 15-79 Kg]. Catheterizations were interventional in 10 patients (62.5%) and for diagnostic purposes in 6 patients (37.5%) (table1). Hypnosis indications were general anesthesia (GA) contraindication in 4 patients (25.0%), the need of accurate pressures measurements without GA interference in 2 patients (12.5%) and interventionist/patients preferences in 10 patients (62.5%). In one patient of 4 years old, the hypnotic status was not achieved and the procedure was aborted before the installation. Procedures were accomplished successfully in 15 patients (93.7%) without any additional sedation even in challenging cases; large atrial septal defect (ASD) closed with 39 mm Occlutech device in 16 years old patient, and catheterization in 14 years old patient with Fontan failure, elevated pulmonary vascular resistances, cyanosis (Hemodynamic Vulnerability Score=5) with GA contraindication. Median procedures and fluoroscopy times were 67.5 min and 5.3 min respectively. In one case, pulmonary artery pressures normalized comparing to previous catheterization under local anesthesia alone leading to the cancellation of cardiac surgery on mitral stenosis. VAS score was under 5/10 in all patients. The ANI remained above 50 (non painful zone) in all but one patient. No significative decrease of the ANI was found during the intervention comparing to baseline (p=0.62). One patient with language difficulties had short and transient decrease of the ANI (49) during one minute after the puncture. No complications were recorded.

**Conclusion:** Paediatric CC are feasible under hypnosis even in complicated cases. Hypnosis was efficient to manage pain and stress in all cases, it ensures more reliable pressures measurements

**VENDREDI 1ER AVRIL 2022**
**SESSION PARALLÈLES « CAS CLINIQUES COMPLEXES »**

- **CARDIOMYOPATHIES**

ADER Flavie

**Echec du séquençage des régions codantes et rôle décisif de l'analyse de transcrits pour résoudre une suspicion de maladie de Fabry chez un patient avec cardiomyopathie hypertrophique**

**Auteurs :**
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**Abstract :**
**Introduction** : La maladie de Fabry est une maladie liée à l'X, causée par des variants pathogènes du gène *GLA* conduisant à une activité alpha-galactosidase réduite.
**Objectif :** Nous rapportons ici un cas d'une suspicion de maladie de Fabry dont le diagnostic a été attesté de façon non conventionnelle, grâce au séquençage de l'ARNm
**Matériel et méthode**
Nous rapportons le cas d'un patient de 44 ans présentant une cardiomyopathie hypertrophique associée à une insuffisance rénale chronique (DFG : 57 mL/min.1,93m$^2$ ), une cornée verticillée et des microanévrismes des vaisseaux de la conjonctive bulbaire évoquant un diagnostic clinique de maladie de Fabry. Le dosage d'alpha-galactosidase est réduit (12 nmol/h/mg prot (N : 20-60) avec un dosage du globotriaosylsphingosine (lyso-Gb3) substrat de l'enzyme augmenté 10,1 nM (N < 0,8) ; arguments biologiques en faveur de la maladie de Fabry.

**Résultats**
Toutefois, l'étude des régions codantes du gène GLA (Séquençage Sanger et séquençage haut débit), et la recherche de délétion intronique se sont avérées négatives. L'analyse de transcrits (ARNm) a finalement révélé un transcrit anormal avec rétention de 57 nucléotides causée par le variant génomique hémizygote c.640-801G>A.
**Conclusions**
Le séquençage haut débit d'un grand nombre de gènes est puissant de par son exhaustivité, mais peut être pris en défaut car certaines régions ne sont pas/ou mal séquencées. Ainsi, dans un contexte de suspicion clinique et/ou biologique de maladie de Fabry avec analyse des régions codante négative, l'effort diagnostic doit être poursuivi et inclure l'analyse de transcrits, permettant un conseil génétique et une discussion thérapeutique aussi précise que possible.

## DI FILIPPO Sylvie

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**Acute myocarditis in children: features and outcomes of COVID-19 and non-COVID patients**

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The objective of the study was to assess the features of acute myocarditis and compare Covid19 and non-Covid19 cases.
Methods : Patients <18y with acute myocarditis (proved by virology and/or MRI and/ or complete recovery of myocardial function) were included. Clinical data, echocardiographic parameters and outcomes were collected. Cases were divided in groups I (non-Covid), II (Covid).
Results : From 1983 to 2021, 139 patients were included : 76 patients in group I and 63 in group II, 67males (31 in group I= 40% vs 36 in II= 57%). Mean age at diagnosis was 6.8 years: 4.2 years in group I vs 9.9 years in II. Heart failure (HF) was present at onset in 78% of cases in group I and 50% in group II: severe HF was more frequent in group I, chest pain was more frequent in II. Mean LVSF at diagnosis was 23.8%: 18.4% in groups I vs 31.6% in II ($p<0.05$). Mitral regurgitation was present in 63.8% of cases= 76.5% vs 43.8% respectively in groups I and II, pericarditis in 16.4% (no difference between groups), thromboembolic events occurred in 7% and arrhythmias in 10% ((all in group I). Virus was positive in 37.5% in group I and SARS-Cov2 positive in all of group II. Inotrope support was needed in 47%, mechanical circulatory support in 8% of cases in group I only. Eleven patients died in group I (within 2months after diagnosis), no death occurred in group II. One was transplanted(3rdmonth) and 19 have sequellae in group I. Complete recovery occurred in 74% of all cases: 40 of group I (58%) and all of group II (100%): time to recovery was longer in group I ( 2 years) than in group I (2 weeks). Mean LVSF improved from 18.4% at onset, to 24.6% at 1stmonth, 26.5% at 3rdmonth, 30.7% at 6thmonth and 38% at last FU in group I, while mean LVSF normalized within 2 weeks after onset in group II.
Conclusion: Acute myocarditis in children has overall favourable outcomes despite early mortality in non-COVID. Myocardial dysfunction and heart failure were less frequent, and complete recovery occurred promptly in COVID cases, while myocardial improvement progressed slowly within the first 6months and beyond in only half of non-COVID cases.

## JABER Mohamed

**Cardiomyopathie restrictive et arthrogrypose**

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**Introduction** : Les variations pathogènes du gène *FLNC* sont impliquées dans la survenue de myopathies et de cardiomyopathies. De précédentes études ont observé des variants plutôt nonsens en

cas de cardiomyopathie dilatée et faux-sens en cas de cardiomyopathies hypertrophiques ou restrictives (CMR). (1)

Deux variations *FLNC* probablement pathogènes (p.A1186V et p.A1183L), très proches l'une de l'autre, ont été rapportées chez 4 enfants atteints de CMR et de myopathie des ceintures, associées dans 3 cas à une arthrogrypose, et dans un cas à une atteinte neurologique. (1)

Nous rapportons une observation identique :
Mat. né à 38 SA, pesait 2,880 kg (23ème per). Le caryotype fœtal (amniocentèse pour risque combiné à 1/70) était normal : 46 XY.
Dès la naissance ont été constatés :

- Une arthrogrypose, une faiblesse musculaire (panel de gènes des arthrogryposes, biopsie musculaire, bilan métabolique normaux, ACPA : variation non pathogène sur le chromosome 19 : duplication en 16q13.33 de 192 KB, héritée de la Maman, asymptomatique)
- Un syndrome pyramidal : IRM médullaire normale, cérébrale : atrophie cortico-souscorticale.
- Une ectopie testiculaire et des hernies inguinales opérées à 2 mois.

Des difficultés alimentaires, apparues dès 3 mois, ont imposé le recours à une gastrostomie à 10 mois.
Mat. a tenu assis à 21 mois.
A 28 mois, un accident vasculaire ischémique sylvien droit associé à des signes d'insuffisance cardiaque a conduit au diagnostic de CMR.
Un traitement diurétique et anticoagulant a permis une « stabilisation » clinique.
Le panel élargi des gènes des cardiomyopathies a retrouvé la mutation hétérozygote p.Ala1186Val (NM_001458.4 :c.3557C>T) du gène *FLNC*.

A 6 ans ½, Mat. ne marche pas, a un très bon niveau de langage, mais des troubles du spectre autistique.
Son insuffisance cardiaque nécessite la poursuite des diurétiques. Il ne fait pas de trouble du rythme.
Il a des séquelles de son hémiplégie, une épilepsie.

**Conclusion** : L'association d'une arthrogrypose, de troubles neuromusculaires et d'une CMR peut être expliquée par des variations pathogènes du gène *FLNC*.
Le regroupement d'observations identiques pourrait améliorer la connaissance de ces pathologies et l'information des patients et de leurs familles.

(1) Kiselev A et Al. Human Mutation 2018 ; 39-1161-72

## JOUADI Hajer

**Molecular Autopsy and Family Screening in a Case of Sudden Cardiac Death reveals Hypertrophic/Dilated Cardiomyopathy and Noonan Syndrome in the same Family**

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**Abstract (Cardiomyopathies)**

**Background**

Genetic cardiac diseases are the main trigger of sudden cardiac death (SCD) in young adults (35 years and under). SCD is defined as an unexpected death of an apparently healthy person, not attributable to an extra-cardiac cause, usually within 1 hour of symptom onset.
Hypertrophic cardiomyopathy is the most leading cause of SCD in young adults. In pediatric cases, HCM is mostly associated to syndromes such as Noonan syndrome. HCM is defined by increased left ventricular wall thickness in the absence of other loading conditions.
Herein, we report a family with a marked history of SCD focusing on one SCD young adult case and his nephew with a syndromic HCM.

**Aims**

The aim of our study was to determine the underlying cause of the SCD in the family and to aid the clinical diagnosis of the syndromic HCM in the pediatric case.

**Methods**

A postmortem Whole Exome Sequencing (WES) was performed for the deceased young adult and a WES for the pediatric patient.

**Results**

For the deceased patient, postmortem WES revealed a missense variant in *ACTN2* gene: c.355G>A; p.Ala119Thr confirming the mixed hypertrophic/dilated cardiomyopathy phenotype detected in the autopsy. This variant has been reported previously in two families with a wide range of cardiac phenotypes such as HCM, DCM, left ventricular non-compaction, and sudden cardiac death.
For the pediatric case, WES allowed us the identification of a novel frameshift variant in *LZTR1* gene: c.1745delT; p. (Val582Glyfs*10) which confirms the clinical suspicion of HCM related to Noonan syndrome. Familial segregation by Sanger sequencing showed that the *LZTR1* novel variant occurred *de novo*.
The *ACTN2* variant was not identified in the pediatric patient. Genetic counseling and testing for the *ACTN2* variant were proposed for the deceased patient (III-3) maternal family branch.

**Conclusion**

The current study highlights the utility of postmortem WES in the identification of causative gene variants underlying SCD. Thus, we report an additional case with the *ACTN2*: p. Ala119Thr variant which may aid a deeper understanding of *ACTN2*-related cardiac phenotypes and SCD risk assessment. Moreover, our study sheds the light on the importance of a thorough clinical examination which allowed us to suspect a syndromic HCM occurring in the same family, namely the Noonan syndrome confirmed then by the identification of a novel frameshift variant in *LZTR1*gene.

## SELEGNY Maelle

Présentation clinique :

Patient de 14 ans suivi pour une myopathie de Duchenne, admis aux urgences pédiatriques pour douleurs thoraciques inhabituelles. Il a comme traitement coversyl, une corticothérapie au long cours par ZAMENE, CALTRATE, GENOTORM. La dernière ETT était normale, FEVG 65%. Il ne présente aucun syndrome infectieux, vaccination covid réalisée plusieurs mois avant, pas de contage. La douleur est constrictive, continue sans irradiation, non modifiée par la position ni par la toux, rétrosternale. L'hémodynamique est normale, sans signe de choc cardiogénique, FC 93 bpm, TA 110/66mmHg, saturation 100% en air. L'examen clinique sans particularité
L'ECG (**figure 1**) retrouve des caractéristiques liées à la maladie de Duchenne et est superposable aux précédents.

Le bilan biologique ne retrouve pas de syndrome inflammatoire mais une Troponine Ic 9500 contrôlé à 41038 ng/l CPK 200, la myoglobine était également augmentée à 324ng/ml, Nt proBNP normaux.

ETT : altération minime de la FEVG à 55% en Simpson bi plan, SGL : 15,6% avec altération du Strain en inféro-basal et inféro-latéral médian, (**Figure 2)**. FEVD normale.

IRM : confirme la myocardite aiguë avec un œdème myocardique ainsi qu'une prise de contraste tardive. Figure 3

Traitement : poursuite de la corticothérapie et majoration traitement de l'insuffisance cardiaque par béta bloquant et Aldactone.
L'évolution a été rapidement favorable sur la biologie et les douleurs mais persistance à l'ETT d'une altération de la FEVG.

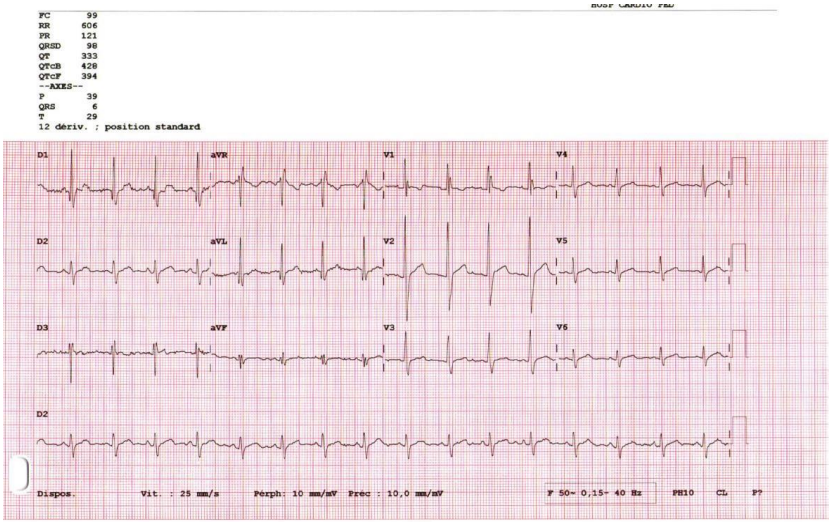


*Figure 1 : ECG : Onde R/S > 1, onde Q en D1 et AvL.*

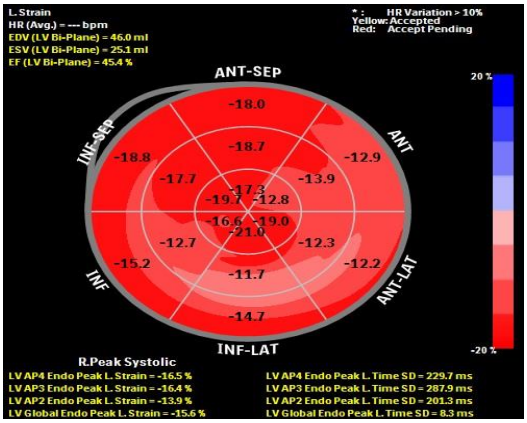


*Figure 2: Strain longitudinal global. SLG altéré à – 15,6%, prédominant en inféro-latéral médian.*

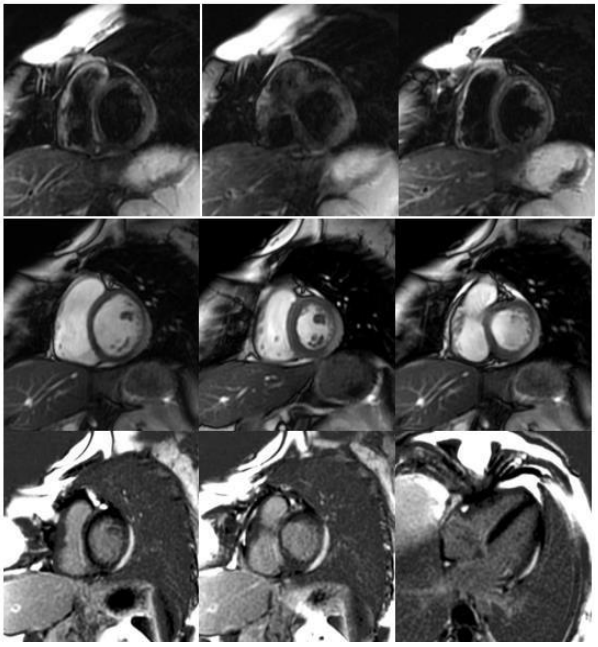

*Figure 3 IRM myocardique. Œdème myocardique de la paroi inféro-latérale basale séquences pondérée en T2. Prise de contraste tardive sous épicardique de siège antéro-latéral basal, inféro-latéral basal et inféro-latéral médian Séquence de réhaussement tardif*

Discussion :

La maladie de Duchenne (MD) est une dystrophinopathie dont l'évolution est marquée par une dystrophie musculaire prédominant au niveau des muscles des ceintures. L'atteinte cardiaque est quasiment constante dès la fin de l'adolescence[1].

Cependant, certains patients semblent se dégrader plus rapidement. Dans une étude[2], ils ont comparé des patients suivis pour une MD, avec et sans rehaussement tardif à l'IRM. Au cours de l'année les 6 patients avec rehaussement tardif à l'IRM ont présenté une dégradation rapide de la fonction ventriculaire gauche, une dilatation du VG et des arythmies. Au cours de la deuxième année de suivi, 2 sont décédés d'une tachycardie ventriculaire et les 4 autres patients sont en insuffisance cardiaque terminale. Les autres patients avec MD sans atteinte myocardique à l'IRM sont restés stables au cours de ces deux années de suivi.

Ainsi le diagnostic de myocardite chez les patients MD semble être un facteur prédictif majeur mais est complexe à affirmer.

- Premièrement, ce sont des patients pauci symptomatiques. Dans notre exemple, le patient a présenté des douleurs thoraciques mais les douleurs thoraciques chez les patients DM sont fréquentes et ont longtemps été dites d'origine musculosquelettique.
- Deuxièmement l'ECG peut être difficile présente chez ces patients des troubles de la repolarisation notamment des ondes Q en DI AVL mais aussi en V5 V6[3].
- La troponine Ic chez ces patients peut être augmentée sans pour autant qu'une atteinte cardiaque soit retrouvée [4]. Il semblerait cependant qu'un taux de troponine > 7.6050 ng/L soit corrélé à une atteinte cardiaque [5], ce qui est largement inférieur au taux de ce patient.

L'IRM semble l'examen des choix pour le diagnostic mais il convient de rappeler que l'étude de Hor et al [5] avait déjà évalué la prévalence d'un rehaussement tardif au sein de patient DM. Plus les patients étaient âgés, plus la prévalence et l'importance du rehaussement tardif augmente.

S'agissait-il réellement d'un épisode de myocardite aiguë ou ces lésions étaient-elles le reflet son atteinte cardiaque liée à la MD ?

Il est impossible de répondre avec certitude à cette réponse. On peut seulement soulever deux éléments : la cinétique de la troponine (figure 4) ainsi que l'œdème myocardique (figure 3) présent en plus du rehaussement tardif. Des biopsies auraient permis de poser un diagnostic histologique plus précis mais il s'agit d'un examen invasif non dénué de complication qui n'a pas été réalisé ici. On peut cependant noter que dans l'étude de Mavrogeni[2], la réalisation de ces biopsies avait retrouvé un phénomène actif que chez un seul patient sur les 6. Enfin, les patients présentant un déficit en dystrophine sembleraient plus à risque de développer une myocardite aiguë en cas d'infection à entero-rhinovirus [6]

En conclusion : l'histoire naturelle de l'atteinte myocardique dans la MD est inconnue et si elle est une constante, certains patients semblent s'aggraver plus rapidement que d'autre. Existe-t-il une prédisposition aux myocardites chez ces patients MD qui pourraient précipiter l'atteinte cardiaque ? Des études supplémentaires sont nécessaires.

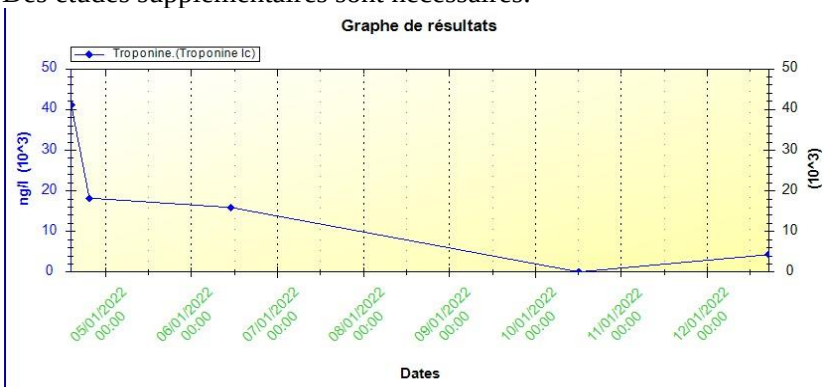


*Figure 4 : Cinétique de la troponine Ic*

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PANAIOLI Elena

**Pulmonary artery banding for severe dilated cardiomyopathy in early childhood** **Authors: Panaioli E[1]., Legendre A[1]., Regis G.[1], Bonnet D[2], Pontailler M[1]. , Khraiche D.[1]**

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2. MD PhD Unité médico-chirurgicale de cardiologie congénitale et pédiatrique, centre de référence des maladies cardiaques congénitales complexes - M3C, Hôpital universitaire Necker-Enfants Malades, Université de Paris, France

**Background:** Paediatric dilated cardiomyopathy (DCM) causes cardiac death especially if the left ventricular end-diastolic diameter exceeds a z score of +5, heart transplantation being the only viable life-saving option. However, this therapeutic option is limited by donor availability and an unpredictable long-term survival. Pulmonary artery banding has been recently proposed as a bridge or alternative to transplantation for DCM when right ventricular function is preserved. The geometric rearrangement of LV dimension is accomplished by modifying the interventricular septal position with hopefully improvement of LV ejection fraction.

**Aims**: we report a series of surgical pulmonary artery banding (PAB) in children with end-stage DCM with preserved right ventricular function or left ventricle aneurysm associated with severe left ventricular dysfunction.

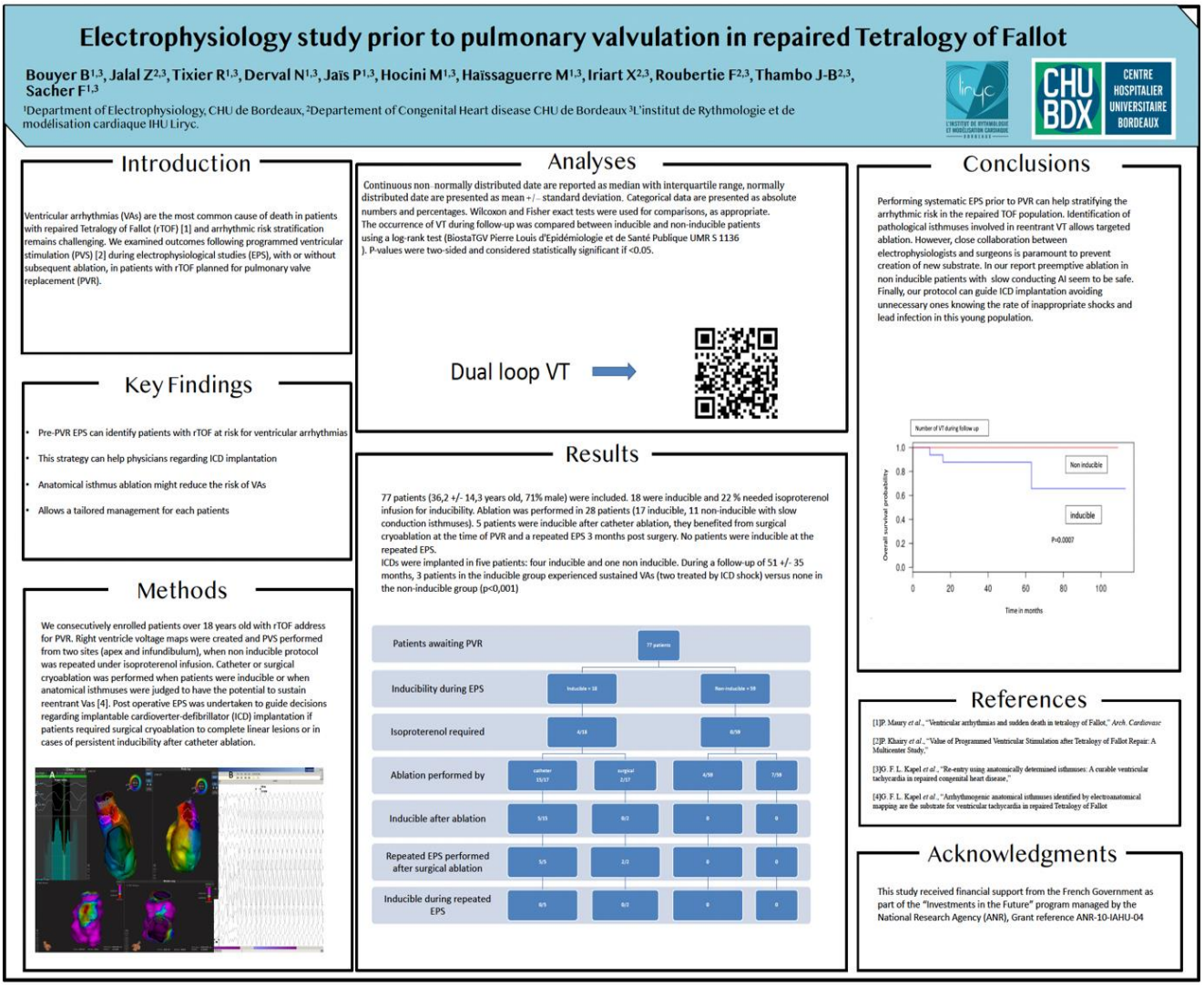
**Methods**: 8 patients with severe DCM had received PAB between 2016 and 2020: 5 had heritable DCM and 3 had idiopathic left ventricle aneurysm associated with severe left ventricular dysfunction. We collected demographic, biological and echocardiographic data (left ventricle end diastolic diameter LVEDD, left ventricle ejection fraction LVEF) prior to surgery, at 6 months, and 1 year after surgery.

**Results**: Median age at PAB was 1.03 ±0.49 years. Two patients out of eight died two months after PAB because of worsening heart failure. One had a PAB at 2 years and the other one had an apical aneurism of left ventricle with LV dysfunction diagnosed before birth. For the 6 surviving patients, (median age at PAB was 0.97±0.26), there was a significant decrease of LVEDD (z score value 8.76± 3.36 vs 2.92±2.82; p=0.005) and trend in improvement of LVEF (32±8 vs 45±13.8 %; p=0.17). After one year, LVEDD was further decreased (z-score; -0,61±3,47 p=0.034) and LVEF also improved to reach 51±13.2% (p=0.02). Two patients needed partial percutaneous dilatation of their pulmonary banding, respectively 1 year and 5 years after the PAB.

**Conclusions:** Positive left ventricle remodelling occurs in the mid-term post-operative period after PAB in patients with severe dilated cardiomyopathy performed before the age of 1 year. The possible impact of these results on long-term prognosis needs to be evaluated.

- **CARDIOPATHIES CONGÉNITALES COMPLEXES**

## BOUYER Benjamin



# Electrophysiology study prior to pulmonary valvulation in repaired Tetralogy of Fallot

Bouyer B[1,3], Jalal Z[2,3], Tixier R[1,3], Derval N[1,3], Jaïs P[1,3], Hocini M[1,3], Haïssaguerre M[1,3], Iriart X[2,3], Roubertie F[2,3], Thambo J-B[2,3], Sacher F[1,3]

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## Introduction

Ventricular arrhythmias (VAs) are the most common cause of death in patients with repaired Tetralogy of Fallot (rTOF) [1] and arrhythmic risk stratification remains challenging. We examined outcomes following programmed ventricular stimulation (PVS) [2] during electrophysiological studies (EPS), with or without subsequent ablation, in patients with rTOF planned for pulmonary valve replacement (PVR).

## Key Findings

- Pre-PVR EPS can identify patients with rTOF at risk for ventricular arrhythmias
- This strategy can help physicians regarding ICD implantation
- Anatomical isthmus ablation might reduce the risk of VAs
- Allows a tailored management for each patients

## Methods

We consecutively enrolled patients over 18 years old with rTOF address for PVR. Right ventricle voltage maps were created and PVS performed from two sites (apex and infundibulum), when non inducible protocol was repeated under isoproterenol infusion. Catheter or surgical cryoablation was performed when patients were inducible or when anatomical isthmuses were judged to have the potential to sustain reentrant Vas [4]. Post operative EPS was undertaken to guide decisions regarding implantable cardioverter-defibrillator (ICD) implantation if patients required surgical cryoablation to complete linear lesions or in cases of persistent inducibility after catheter ablation.

## Analyses

Continuous non-normally distributed date are reported as median with interquartile range, normally distributed date are presented as mean +/- standard deviation. Categorical data are presented as absolute numbers and percentages. Wilcoxon and Fisher exact tests were used for comparisons, as appropriate. The occurrence of VT during follow-up was compared between inducible and non-inducible patients using a log-rank test (BiostaTGV Pierre Louis d'Epidémiologie et de Santé Publique UMR S 1136 ). P-values were two-sided and considered statistically significant if <0.05.

Dual loop VT

## Results

77 patients (36,2 +/- 14,3 years old, 71% male) were included. 18 were inducible and 22 % needed isoproterenol infusion for inducibility. Ablation was performed in 28 patients (17 inducible, 11 non-inducible with slow conduction isthmuses). 5 patients were inducible after catheter ablation, they benefited from surgical cryoablation at the time of PVR and a repeated EPS 3 months post surgery. No patients were inducible at the repeated EPS.
ICDs were implanted in five patients: four inducible and one non inducible. During a follow-up of 51 +/- 35 months, 3 patients in the inducible group experienced sustained VAs (two treated by ICD shock) versus none in the non-inducible group (p<0,001)




## Conclusions

Performing systematic EPS prior to PVR can help stratifying the arrhythmic risk in the repaired TOF population. Identification of pathological isthmuses involved in reentrant VT allows targeted ablation. However, close collaboration between electrophysiologists and surgeons is paramount to prevent creation of new substrate. In our report preemptive ablation in non inducible patients with slow conducting AI seem to be safe. Finally, our protocol can guide ICD implantation avoiding unnecessary ones knowing the rate of inappropriate shocks and lead infection in this young population.




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## Acknowledgments

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## DI FILIPPO Sylvie

**Management and outcomes of coronary fistulae in children and young adults**

Thomas Perouse De Montclos, Mohamed Bakloul, Olivier Metton, Claire Galoin Bertail, Fanny Deville, Diane
Ouvrier Buffet, Cecile Leconte, Sylvie Di Filippo Department of Congenital Heart Disease, Claude Bernard University, Lyon, France

BACKGROUND AND AIM:The objective of this study was to assess anatomical characteristics, management and oucome of coronary artery fistulaes (CAF) diagnosed at childhood age. METHODS:Retrospective observational
single-centre study included all pediatric patients diagnosed with CAF from 2011 to 2014. Demographics, clinical, echocardiographic data, therapeutic management and outcomes were assessed. RESULTS:Eighty five patients were included in the study, 51 males and 34 females, diagnosed at a mean age of 6.5 years. Only one coronary artery was involved in 93% of the cases and 91% connected coronary artery and right heart (50% right ventricle, 35% main pulmonary artery and 6% right atrium.

CAF was congenital in 89% of cases, acquired after surgery in 11%. CAF was isolated in 58% or associated with congenital heart disease in 42% of the cases. Coronary artery was enlarged in 27% and increased pulmonary flow was present in 8% of the cases. Symptoms and/or heart murmur were present in respectively 3 cases (4%) and 51% of the cases. Diagnosis was made by echocardiographic and Doppler evaluation. CT scan was performed to reach diagnosis in 11% of patients and coronary angiography in 6%. No patient died. Only 2 patients (2.3%) underwent closure of CAF (1 interventional procedure and 1 surgery).
CONCLUSIONS:Coronary artery fistulae natural history is uncomplicated and uneventful in the vast majority of cases.

### Necrotizing enterocolitis and congenital heart disease

Claire Galoin Bertail, Cecile Leconte, Diane Ouvrier Buffet, Fanny Deville, Julia Mitchell, Olivier Metton, Mohamed Bakloul, Thomas Perouse De Montclos, Sylvie Di Filippo Department of Congenital Heart Disease, Claude Bernard University, Lyon, France

**Background:** Congenital heart disease represents a risk factor for necrotizing enterocolitis
**The objectives** of the study were to describe and compare the population of infants with congenital heart disease and digestive symptom complicated or not by necrotizing enterocolitis, and assess the risk factors.
**Methods:** Between January 2016 and December 2020, retrospective analysis of data in infants with congenital heart disease under 3 months of age diagnosed with digestive symptom complicated or not by a necrotizing enterocolitis. The population was divided into two groups: “NEC group” (infants with necrotizing enterocolitis) “No-NEC group” (infants with an isolated digestive symptom, but no necrotizing enterocolitis)
**Results**: Overall 67 patients were included in the study: 36 in the NEC group and 31 in No-NEC. The prevalence of enterocolitis during the study period was 4%. Underlying congenital heart disease included coarctation of the aorta, pulmonary atresia and transposition of the great arteries. Fourtyfive patients (67%) were administered prostaglandins infusion, 49 (67%) had an umbilical venous catheter, while 67,2% underwent cardiac surgery, 38,8% percutaneous interventional catheterization and 11,9% had no intervention. Digestive events occurred more often within the pre-interventional period ($p < 0.05$) but necrotizing enterocolitis was not more frequent than benign digestive symptoms, although all the infants were fed. Patients were older and cardiac intervention was performed later in the NEC group than No-NEC group ($p < 0.05$). Mother’s own milk was less frequently used in NEC patients than No-NEC (40.7% versus 60%, ns). The incidence of hypotroph newborns, high-calorie milk formula and use of antibiotics was greater in NEC than No-NEC group ($p < 0.05$). There was no significant difference in gestational age and transfusion between groups. Twenty-eight cases (48%) occurred in early course after surgical or percutaneous procedure: necrotizing enterocolitis tended to be more frequent in cases (43.3%) who underwent "palliative" surgery or prolonged discontinuation of prostaglandin than in those who had complete surgical repair (61.5% vs 47%, ns).
**Conclusion**: The enterocolitis in congenital heart disease may due to an abnormal blood flow to the mesenteric vessels. Cardiac procedure should not be delayed, in order to prevent preoperative enterocolitis. Feeding does not increase the incidence of enterocolitis infants and the administration of mother’s own milk or donor human milk should be promoted in this population.

## CAS CLINIQUE COMPLEXE

**Cardiomyopathie familiale par non-compaction chez un nouveau-né avec mutation PKP2 :** nécrose myocardique néonatale, options thérapeutiques et pronostic

**Long-Term Outcomes of Transcatheter Potts Shunt in Children with Suprasystemic Pulmonary Arterial Hypertension**

**Raymond N. HADDAD[1],** Maryline LEVY[1], Isabelle SZEZEPANSKI[1], Sophie MALEKZADEHMILANI[1], Damien BONNET[1]

[1]M3C-Necker, Hôpital Universitaire Necker-Enfants malades, AP-HP, Paris, France.

**Introduction:** Transcatheter Potts shunt (TPS) is identified as effective palliation for children with severe pulmonary arterial hypertension (PAH). Debates on the long-term outcomes remain unsolved.
**Objectives:** We evaluate the long-term outcomes of the largest experience with TPS with a focus on the durability of the implanted material.
**Methods:** Retrospective data review was obtained from children with severe PAH who have undergone TPS at our institution between 2009 and 2018. Early censored individuals were excluded. Long-term outcomes of procedure survivors were comprehensively evaluated. **Results:** Thirteen patients (53.8% males) were identified. TPS was performed with bare-metal stenting of restrictive/probe arterial duct (n=7) or created by radiofrequency vessel perforation/covered stenting (n=6). Improvement in overall clinical condition was significant at discharge ($p<0.001$), inconsistent across follow-up, but remained significantly improved at the last visit ($p<0.05$). Improvement in functional status was significant ($p<0.001$). There was no significant

gradual improvement in other disease markers (TPASE, 6MWD z-scores, and NT-proBNP levels). 57.1% of patients initially under prostanoid therapy were weaned but reduction in the overall need for PAH medications was not significant. Median follow-up was 62.7 months (IQR, 32.2-96.5 months). One patient died 28.5 months postoperative after a severe viral infection. Survival was 100% at 1 year and 92.3% at 5 years. Freedom from reinterventions was 77% and 17% at 1 year and 5 years, respectively. Stent malfunctioning indicated balloon dilatation (46.1%) and re-stenting (38.5%). One patient is listed for heartlung transplantation.
**Conclusions:** Survivors of TPS procedures experience significant improvement in functional class that can be durable and potentially free from prostanoid. Clinical worsening and stent malfunctioning are frequent morbid events indicating recurrent transcatheter reinterventions throughout follow-up. Five-year survival is however satisfactory.

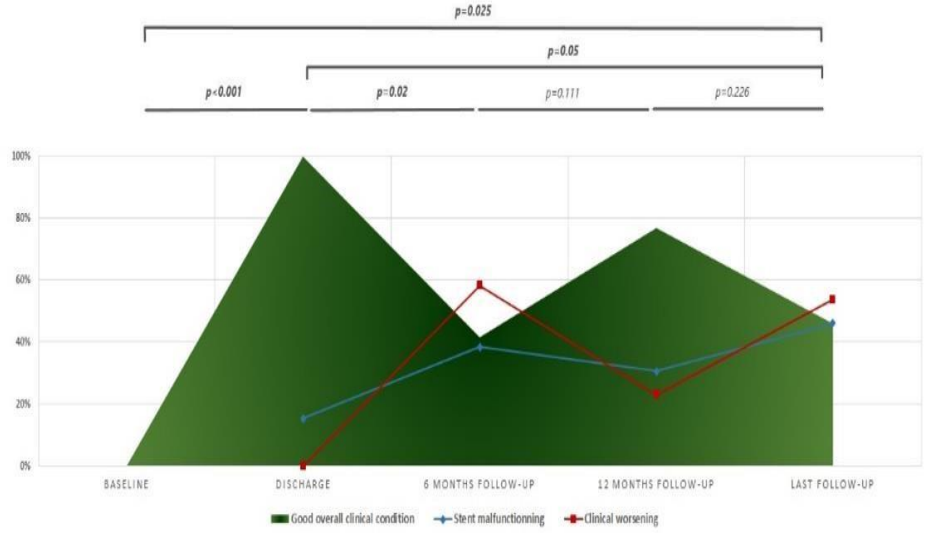


Fig .1 Progression of overall clinical status across follow-up

*Clinical worsening is defined by the presence of at least one of the following: 1) worsening in world health organization- Functional class (WHO-FC); 2) NT-pro BNP ≥1400 pg/ml; 3) tricuspid annular plane systolic excursion (TAPSE) ≤15mm; 4) increase or adjunction of diuretics; and 5) adjunction of new pulmonary arterial hypertension specific medical therapy.*

*Stent malfunctioning is defined as maximum velocity on stent >2 m/s*

## SILINI Alexandre

**Percutaneous edge-to-edge repair of severe tricuspid valve regurgitation in high-surgical risk patients with systemic right ventricle: A multicenter French cohort study (PETER TRESRIV)**

**Authors:** Alexandre Silini, Patrice Guerin, Zakaria Jalal, Jean-Benoit Thambo, Pascal Amedro, Valentin Femeni, Robin Le Ruz, Charlène Bredy, Helene Bouvaist, Xavier IRIART

**BACKGROUND**:
Patients with systemic right ventricle (SRV) (usually congenitally corrected transposition of the great arteries or transposition of the great arteries corrected by atrial switch) commonly develop significant systemic tricuspid valve regurgitation and systemic right ventricular dysfunction in adulthood, both of which present a therapeutic dilemma. Until recently, the only therapeutic option has been surgery, but the rate of complications is high. Percutaneous edge-to-edge repair may represent an alternative, especially for high-surgical risk patients.

**METHODS**:
Ten high-risk surgical patients with severe systemic tricuspid regurgitation (TR) undergoing percutaneous repair with the MitraClip or TriClip system (Abbott) were enrolled in the study between May 2019 and October 2021. We collected and compared clinical (symptoms, quality of life questionnaires), biological (renal function, BNP/NT-proBNP levels), VO2 max, echocardiographic, and cross-sectional imaging (TR severity, right ventricle dilatation, and dysfunction) data at baseline and 6 months after the procedure.

**RESULTS**:
We report a percutaneous implant success rate of 80%, one early death due to septal leaflet tear, and two successfully ablated common flutters. Clinically, we observed an improvement in functional status after 6 months, as well as in the median physical (+10.3 points) and mental (+12.2 points) quality of life

scores. The median levels of B-type natriuretic peptide and NT-proBNP in the blood decreased by 162 and 178 µmol/L, respectively. VO2 max did not change significantly. The effective regurgitant orifice area and regurgitation volume improved by 20 mm² and 11 mL, respectively, while the median SRV volume, as measured by magnetic resonance imaging or tomodensitometry, decreased by 25 ml/m² and 22 ml/m² (diastolic and systolic volumes, respectively). The right ventricle ejection fraction increased by 18.5%.

**CONCLUSIONS**:
Percutaneous edge-to-edge repair of systemic TR might be a safe and effective therapeutic option in high-risk adult surgical patients.

## TAJOURI Asma

**Inferior sinus venosus defect and anomalous hepatic venous return to the coronary sinus leading to an Eisenmenger syndrome.**

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### Background

Inferior sinus venosus defect associated with left hepatic vein drainage to the coronary sinus is an extremely rare condition. We report the case of a 41-year-old man suffering from pulmonary arterial hypertension related to this unusual congenital heart disease.

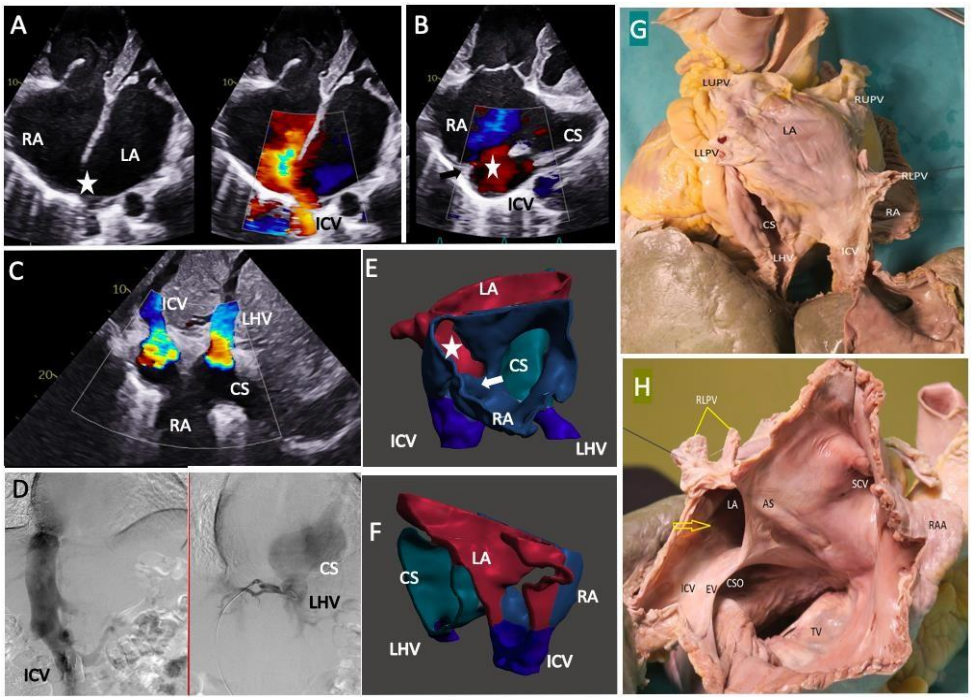
### Case Report

A 41-year-old man with pulmonary arterial hypertension due to an inferior sinus venosus defect was referred for heart-lung transplantation. He complained of congestive heart failure and WHO-NYHA 3 dyspnoea. Right ventricle (RV) ejection fraction on MRI was lowered to 18% with enlarged right cavities (end diastolic RV volume: 228 ml/m², right atrium area: 50 mm²). Under specific therapy (tadalafil and ambrisentan), pulmonary vascular resistance was 6.2 Wood unit.m². Mean atrial pressures were highly elevated at 22 mmHg. Inferior sinus venosus defect consisted of an overriding of the inferior caval vein (ICV) over the interatrial septum, nicely depicted on a 3D model (panel E & F), with a large

interatrial defect (panel A, B, E & F ; star) and continuity between the ICV and the posterior wall of the left atrium (panel A). A prominent Eustachian valve (panel A; arrow) on the right side of the ICV directed the flow preferentially to the left atrium. An intriguing left hepatic vein (LHV) anomalous return to a dilated coronary sinus was diagnosed (panel C & D). There was an intrahepatic small connection between the ICV and the LHV (panel D). The patient died of terminal heart failure while on the waiting list. Autopsy confirmed the diagnosis of inferior sinus venosus defect by visualizing partial anomalous connection of the two right lower pulmonary veins to the ICV at its junction with the right atrium, and the anomalous drainage of the LHV to coronary sinus (panel G, H).

## Conclusion

LHV drainage to the coronary sinus is an extremely rare and benign congenital vascular anomaly often associated with other vascular malformations such as persistent left superior vena cava, anomalous pulmonary venous drainage, interrupted ICV with azygos continuation. In this case, its recognition was important to plan the heart-lung transplantation.




## Figure's legend

A: TTE (4 chambers view): visualisation of the atrial septal defect (star), and the left and right atriums (LA and RA) dilatated. The atrial septum overrides the inferior caval vein (ICV).
B: TEE (modified 4 chambers view): visualisation of the coronary sinus (CS) opening in RA. Septal defect is marked by the star, and the septum (arrow) overrides the ICV.
C: TEE (sub-costal view): visualisation of the ICV drainage to the RA with the septum over-riding. Visualisation of the left hepatic vein drainage to the CS opened in the RA.

D: angiographic face view: Visualisation of the IVC drainage to RA and the left hepatic vein drainage to the CS. Note the small vein communication between these two veins returns just above the diaphragm area.

## ROORYCK-THAMBO Caroline

### Caractérisation de *HEY2*, nouveau gène candidat de Tétralogie de Fallot

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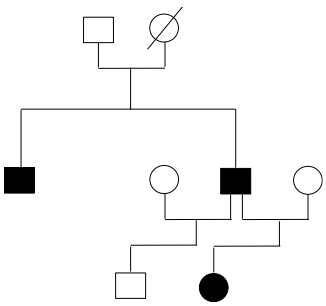
#### Introduction

La Tétralogie de Fallot (T4F) est la cardiopathie congénitale cyanotique la plus fréquente. Seuls de rares gènes sont associés à des formes génétiques de T4F. Nous décrivons une famille avec 3 cas présentant une T4F porteurs un variant faux-sens hétérozygote dans le gène *HEY2*.
*HEY2* est un gène impliqué dans des atteintes cardiaques à type de NCVG (Richard et al. *Clin Genet* 2019), syndrome de Brugada (Veerman et al. *Circ Res* 2017), et récemment décrit dans une famille avec diverses malformations cardiaques congénitales et anévrismes de l'aorte thoracique (Van Walree et al. *Genet Med* 2021). Il n'a jamais été décrit comme associé à la tétralogie de Fallot chez l'homme.



#### Objectif

Nous visons à confirmer l'implication de ce gène HEY2 dans la Tétralogie de Fallot de cette famille, en réalisant la caractérisation fonctionnelle du variant p.(Glu57Asp).

#### Matériel et Méthodes

-Description d'une famille avec trois cas présentant une T4F non syndromique de transmission autosomique dominante
-Séquençage d'un panel NGS de 14 gènes impliqués dans les cardiopathies congénitales
-Etude de l'activité du facteur de transcription HEY2 par la génération du mutant HEY2 et test luciferase

**Résultats**

Un variant hétérozygote faux-sens, NM_012259.2 :c.171G>C/p.(Glu57Asp), a été identifié dans HEY2, facteur de transcription impliqué dans le développement embryonnaire cardiaque. Ce variant entraine une perte de fonction de la protéine HEY2 avec augmentation de l'activité du promoteur de Tbx2, normalement réprimé par HEY2 sauvage, dans un modèle cellulaire. Les souris KO pour HEY2 développent une tétralogie de Fallot, une atrésie tricuspide, une hypertrophie ventriculaire avec désorganisation myofibrillaire (Donovan et al. Curr Biol 2002).

**Conclusion**

Ces données sont en faveur de l'identification de *HEY2* comme nouveau gène de tétralogie de Fallot, dans une forme familiale de transmission autosomique dominante avec caractérisation d'un nouveau variant hétérozygote de type perte de fonction. Ce gène doit être exploré dans les phénotypes familiaux de cardiopathie congénitale, de non compaction du VG et anévrismes de l'aorte thoracique. Cette observation montre aussi l'intérêt de développer des outils fonctionnels pour caractériser les variants issus des données de séquençage haut débit des patients de la filière CARDIOGEN.