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Review article

Cardiac serious adverse reactions in donors in France 2010–21

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ABSTRACT

Aim: To study cardiac serious adverse reactions in blood donors (CSARD) reported in the context of whole blood donation (WBD) or apheresis donation (AD) in France. Although potentially serious, they have been poorly studied so far.

Methods: Retrospective descriptive study of the 125 CSARD (myocardial infarction-MI, acute coronary syndrome-ACS, angina pectoris-AP, rhythm disorder-RD) reported between 2010 and 2021. The studied parameters were age, gender, type of donation, diagnosis, time to onset, imputability, severity (grade), cardiovascular risk factors (CVRF). They were reviewed within the reports by 5 experts, who independently recorded their opinions on each parameter (except age, gender, type of donation). The collegial analysis of the opinions then resulted in a consensus for all cases. The time between the occurrence of CSARD and donation has been extended and limited to 48 h. An additional criterion of imputability was added for the CSARD attributed to causes other than the donation (e.g., coronary atheroma) but Aggravated or Triggered by the donation: AT1 possibly (>24–48 h post-donation), AT2 probably (>12–24 h post-donation) or AT3 certainly (within 12 h or pre-donation start).

Results: Out of 125 reports, 50 were excluded: cardiac qualification of SARD invalidated (8), lack of data (2), absence donation (1), occurrence more than 48 h after the donation (39). The 75 included CSARD (including 5 deaths) comprised 58 coronary events (38 MI, 13 ACS, 7 AP) and 17 RD, and their complementary imputability criterion (AT) was classified respectively as follows 1 (20%), 2 (24%), 3 (56%). The estimated cumulative incidence of CSARD/106 donations is 2.1, significantly higher for AD (5.3) than for WBD (1.6; $p < 0.001$). The male (M) and female (F) percentages are 81% vs 19%, significantly different from the ones of the standard donor population over 2010–21: 48% M vs 52% F. The median ages, 55 years (30–70) in men, and 47 years (23–68) in women, were significantly higher than the ones of standard donor population 2010–21, respectively 46 ($p < 0,001$) and 41 ($p = 0,04$). In the 58 coronary accidents, at least 3 CVRF were noted in 38 cases (66%) and at least 4 CVRF in 20 cases (34%), including 5 with 5 CVRF. In 6/75 cases (8%) pre-existing signs not detected during the pre-donation interview (PDI) would have permanently contraindicated donation.

Conclusions: A complementary study should assess whether a more formalised consideration of CVRF in the PDI could reduce the frequency of CSARD of coronary type.

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Contents

1. Introduction

Although rare, cardiac serious adverse reactions in donors (CSARD) reported in the context of whole blood donation (WBD) or apheresis donation (AD) can have serious consequences for donors. The internationally recognized classification and definitions of donation-related complications include under the term "major cardiovascular event" (MCE) heterogeneous complications: myocardial infarction (MI), cardiac arrest, other acute cardiac symptoms, stroke, or death within 24 h of donation [1]. In the European Union (EU) in 2018 [2] there were 19 MCE or deaths within 24 h reported after a WBD (0.4%) and 10 after an AD (0.7%). In total these 29 reactions represented 0.46% of the 6,239 serious adverse reactions in donors reported in this context. But these data are not comprehensive, due to the fact that the reporting the member states of their SARDs to the EU is carried out on a voluntary basis [2], the overall under-reporting of donation-related complications and the heterogeneity of reporting [3]. And to our knowledge, no specific study on CSARDs has yet been published in the literature confirming the interest of a scientific study on this subject.

For donor safety, given the seriousness of CSARDs, and from a prevention perspective, it is important to look for cardiovascular risk factors (CVFR) that could be detected in the process of selecting prospective donors. But a recent European study shows that with limited or divergent scientific evidence, it remains very difficult to formalise the decision-making process leading to defining donor selection criteria [4].

Finally, the CSARD reports raise questions about the involvement of the donation, about the time frame to be retained in this type of event, and about the evaluation imputability of MI in the presence of causes pre-existing the donation (e.g. atheromatous vascular lesions). In this context, the present study on CSARD reported in France aims to contribute to the advancement of this major concern, with the following three objectives. i) Improve the description of these events by analysing CSARD reported during a WBD or AD in France over a period of 12 years; ii) Look for risk factors that may be identified in these donors before donation with a view to reducing the frequency of CSARD; iii) In terms of haemovigilance practices, check the applicability of diagnostic criteria and additional criterion to the current imputability levels for CSARD reports.

2. Methods

This is an observational retrospective study of the 125 CSARD reported in the French national haemovigilance system between 01/01/2010 and 31/12/2021. Each report was first the subject of an individual analysis by 5 experts, co-authors. Then, their collegial analysis (three 2-hour meetings) allowed each report to be discussed and a consensus to be reached for all the parameters studied (below). Among these 5 co-authors, 2 are anaesthesiology and intensive care specialists, one of whom is also cardiologist, and all 5 are experts in the field of donor haemovigilance.

The diagnoses retained are those established from medical reports and, where applicable, hospitalisation reports collected in haemovigilance surveys. The current definitions of coronary accident diagnoses have been recalled in recent European recommendations [5]. The non-inclusion criteria were lack of data to establish a diagnosis, cardiac qualification of SARD invalidated, absence of donation. A temporal criterion was added to these criteria. The time between the occurrence of CSARD and donation is usually of 24 h [1,6]. In our study, this time has been extended, with a consensus of all authors, and limited to 48 h. The extension of time to 48 h was based on the kinetics of troponins, which is a highly specific biological marker of myocardial damage in myocardial infarction (MI), and showing that they can rise up to 48 h after the first signs [7,8]. After 48 h, the cardiac events are deemed not to be attributable to the donation, and therefore were excluded from the study.

For the records included in the study, the following parameters were studied: diagnosis, time to onset, imputability, severity grade, age, gender, cardiovascular risk factors (CVRF), and type of donation.

The study of imputability levels showed a difficulty in applying the regulatory criteria of national haemovigilance [6] for patients with pre-existing coronary atheroma lesions before donation. In fact, these lesions, not detected during the pre-donation interview (PDI), constitute "convincing elements" which "allow the adverse reaction to be attributed to causes other than the donation of blood or blood components". In the regulation logic, this would lead to excluding the imputability of the donation. However, in these situations, the aggravating (A) or triggering (T) role of the donation can be evoked in the occurrence of the CSARD. This led to designing and applying to the studied cases a complementary criterion to the imputability with 3 levels:

- **AT1:** the donation **possibly** aggravated or triggered the adverse event, when the CSARD occurred between > 24 h and ≤ 48 h after the donation.
- **AT2:** the donation **probably** aggravated or triggered the adverse event, when the CSARD occurred between > 12 h and ≤ 24 h after the donation.
- **AT3:** the donation **certainly** aggravated an CSARD existing before the donation but not detected in the pre-donation interview (PDI), or **certainly** aggravated or triggered the adverse event, when the CSARD occurred within 12 h of the donation.

In the absence of data describing rhythm disorders (RDs apart from those observed during vasovagal reactions (VVR), directly caused by blood or blood component donations, the same approach was applied to assess their imputability. Severity grades were assessed in accordance with national regulation [6]. The CVRF considered for the study were those of the Primary Health Insurance Fund (CPAM) [9], taking up the CVRF of the European recommendations in this area [10]: age and gender (M > 50, F > 60); family history of CV; smoking; diabetes; high blood pressure (HBP) defined as systolic BP > 140 mm Hg and/or diastolic BP > 90; dyslipidaemia (increased LDL cholesterol, decreased HDL cholesterol, increased triglycerides); obesity or overweight defined respectively by a body mass index (BMI) > 30 or > 25 kg/m^2 [11]. Sedentary lifestyle and microalbuminuria, included in this list, were not taken into account. A personal history of CV pathology pre-existing to the donation was added to the CVRF evaluated.

Statistical analyses were performed with R version 4.2.0 (R Foundation for Statistical Computing). We described the distribution of diagnoses for all CSARD studied and by gender. To compare age by gender for each category of CSARD, for all coronary events, and for all CSARD, we used the Wilcoxon-Mann-Whitney test. To compare the incidences of the studied CSARD according to the type of donation (WBD vs AD), we used the Fisher exact test. The distribution of the cumulative number of CVRF was also described for each category of CSARD, for all coronary events, and for all CSARD. A p-value < 0.05 was considered statistically significant. A sensitivity analysis was performed for CSARD with a maximum onset time of 24 h.

3. Results

Of the 125 CSARD reported between 2010 and 2021, 98 (78%) included the opinion of a cardiologist, and 21 (17%) included the opinion of an external non-cardiologist physician. Only 6 reports (5%) did not collect an external medical opinion. The authors' analysis of the reports led to the exclusion of 50/125 reports (39%): 8 for a cardiac qualification of SARD invalidated, 2 for lack of data, 1 for absence of donation, and 39 for a time between the occurrence of CSARD and donation is more than 48 h. In the 75 CSARD included in the study, the diagnoses established were as follows: 38 myocardial infarctions (MI), 13 acute coronary syndromes (ACS), 7 angina pectoris (AP), i.e 58 (77%) coronary accidents (CA), and 17 (23%) rhythm disorders (RD). Coronary angiography or autopsy was able to demonstrate coronary atheromatous lesions in 37/58 (64%) of CA. Such lesions were assessed as probable in view of the context (clinical and stent placement) in 12/58 cases, possible but not proven in 4/58 cases, and were ruled out in 5 cases (normal coronary angiography). Overall, the CA were mostly related to atheroma lesions. The diagnoses established for TR and their functional symptomatology apart from the abnormal pulse (observed on the occasion of palpitations or an irregular pulse on clinical examination) are summarised in Table 1. In 7/17 cases, including 6 sinus tachycardias, the rhythm disorder detected by taking the pulse after the donation was otherwise asymptomatic.

Table 1
Diagnosis and symptoms of rhythm disorders (n = 17).

Diagnosis	N	Clinical signs[1]	Asymptomatic[1]
Sinus tachycardia	7	1 (faintness)	6
VE[2], AE[3]	5	4 (1 CRA[4], 3 faintness)	1
FVTHH[5]	1	1 (chest pain)	0
PAF[6]	1	1 (faintness)	0
AVNRT[7]	1	1 (nausea)	0
Arythmia[8]	2	2 (2 faintness)	0

1 Apart from the DR detected in all cases by taking the pulse. 2. VE: ventricular extrasystoles. 3. AE: atrial extrasystoles. 4. CRA: cardiorespiratory arrest. 5. FVTHH: fascicular ventricular tachycardia in healthy heart. 6. PAF: paroxysmal atrial fibrillation. 7. AVNRT: Atrio-ventricular nodal reentrant tachycardia. 8. Arrhythmia type not reported.

Analysis of the complementary criterion of imputability, with its 3 levels depending on the time to onset, showed a level AT3 (certain) in 42 cases (56%), AT2 (probable) in 18 cases (24%), and AT1 (possible) in 15 cases (20%). Thus, the donation was evaluated as an aggravating or triggering factor of the CSARD of strong level (certain or probable), due to the occurrence within 24 h, for 80% of the CSARD. Among the cases classified as AT3 (certain), the serious event had started before the donation, without being detected by the PDI, in 6/42 cases (14%). In 5 cases (8.6% of CA), it was anginal pain (typical or atypical) between 2 days and 4 months before the donation. In one case it was a pre-existing rhythm disorder.

Over the 12-year study period, a total of 35,055,266 donations were collected from donors in France, including 29,988,323 WBDs and 5,066,943 ADs. These data allow us to estimate the cumulative incidence of CSARD/10^6 donations at 2.14 (95% CI: 1.65–2.62) for all types of donations, 1.60 for WBD (95% CI: 1.15–2.05), and 5.33 for AD (95% CI: 3.32–7.34). Statistical comparison of estimated incidences for WBD vs AD shows (Table 2) a statistically higher incidence of CSARD for AD vs WBD (WBD/AD incidence rate ratio = 0.30, 95% CI: 0.19–0.48, $p < 0.001$). This statistically higher incidence with AD vs WBD is found independently for CA (WBD/AD = 0.30, 95% CI: 0.17–0.51, $p < 0.001$) and RD (WBD/AD = 0.31, 95% CI: 0.11–0.84, $p = 0.03$). The sensitivity analysis, for CSARD with a maximum onset time of 24 h, supports these results for CA ($p = 0.001$) but the test result is at the limit of the significance threshold for RD ($p = 0.05$).

The distribution of CSARD by donor gender and age is presented in Table 3. For the 75 CSARD, the proportion of male (M) was higher than that of female (F), with an M/F ratio of 81% versus 19%. It was 86% versus 14% for the 58 coronary CSARD and 65/35 for the 17 RD CSARD. The percentage observed for CSARD, indicating a clear male predominance, is significantly different from that of the standard donor population over the period 2010–2021: 48% vs 52% [12,13]. Indeed, by applying this average sex ratio, the number of CSARD expected for the period would be 36 for men and 39 for women (chi-2 test of adequacy, $p = 1.1 \times 10^{-8}$). Regarding age, 69.4% of donors were over 50 years old (Fig. 1). The median age of 55 years (30–70) for men, and 47 years (23–68) for women (Table 3) is significantly higher than the median age of standard donor population for the period 2010–21, 46 years for men ($p < 0.001$) and 41 years for women ($p = 0.04$) (source EFS, French national blood service). Furthermore, the statistical comparison of ages (Wilcoxon test) shows no difference between the ages of men and women for CA. On the other hand, for RD the age of women is significantly lower than that of men. The sensitivity analysis, for CSARD with a maximum onset time of 24 h, supports these results for CA and RD.

The severity of the CSARD was grade 4 (death) in 5/75 cases (6.7%), all related to CA, with the following diagnoses and levels of the additional criterion for imputability: 1 AT3 MI (pain 2 days before WBD), 1 AT 3 ACS (9 h after plasmapheresis), 2 AT2 MI (15 and 24 h after WBD), 1 AT1 MI (41 h after WBD). The severity was grade 3 in 70/75 cases (93%) (58 of which required hospitalisation). The severity of RD was lesser than that of CA: no grade 4, and hospitalisation in 5/17 cases (29.4%), vs 53/58 cases (91.4%) in CA (Fisher's exact test, $p = 9.9 \times 10^{-7}$). In the 10 cases of symptomatic RD, only one had a clinical presentation requiring urgent care (cardiorespiratory arrest). In one case of RD, hospitalisation occurred for sinus tachycardia that was otherwise asymptomatic.

The CVRF sought and noted in the 75 reports and post-donation surveys are presented in Tables 4 and 5. Age and a BMI > 25 were noted in 68 and 60% of cases respectively, obesity was found in 16%

Table 2
Types of donations in the CSARD studied.

	Total	Incidence /10^6 donations[1]	WBD	Incidence /10^6 WBD[2]	AD	Incidence /10^6 AD[3]	p WBD vs AD[4]
MI	38	1,08	22	0,73	16	3,16	<0,001
ACS	13	0,37	9	0,30	4	0,79	0,11
AP	7	0,2	6	0,20	1	0,20	1
Total CA	58	1,65	37	1,23	21	4,14	<0,001
RD	17	0,48	11	0,37	6	1,18	0,03
Total CSARD	75	2,14	48	1,60	27	5,33	<0,001

1. 35,055,266 donations over the period 2010–21. 2. 29,988,323 WBD over the period 2010–21. 3. 5,066,943 CE over the period 2010–21. 4. Fisher's exact test.

Table 3
Gender and age of donors in the CSARD studied.

	Total	Male	Female	Age M: median (range)	Age F: median (range)	Age M vs F: p[1]
MI	38	33	5	55 (33–70)	63 (38–65)	0,42
ACS	13	12	1	53,5 (41–67)	42	-[2]
AP	7	5	2	60 (51–67)	60 (52–68)	-[2]
Total CA	58	50 (86%)	8 (14%)	55 (33–70)	60,5 (38–68)	0,80
RD	17	11 (65%)	6 (35%)	55 (30–65)	41 (23–50)	0,03
Total CSARD	75	61 (81%)	14 (19%)	55 (30–70)	47 (23–68)	0,08

1. Wilcoxon-Mann-Whitney test. 2. Too small numbers.

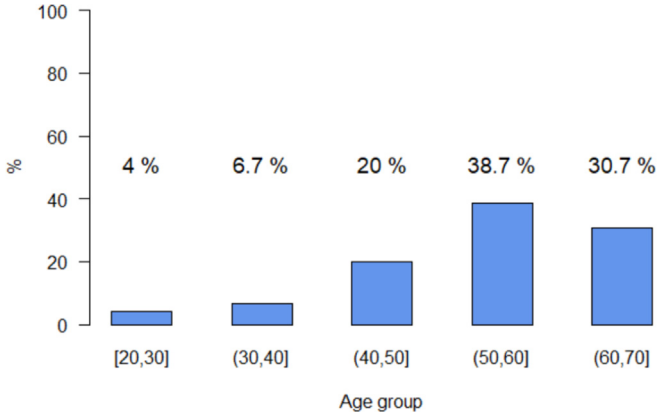

Fig. 1. Distribution of donors with CSARD studied by age group (n = 75).

Table 4
Distribution of cardiovascular risk factors in donors in the CSARD studied (n = 75).

RF	n	%
Age (M > 50 ans / F > 60 ans)	51	68%
BMI > 25	45	60%
Tobacco[1]	33	44%
Dyslipidaemia	22	29%
High blood pressure	17	23%
Family history	16	21%
Diabetes	4	5%
Pre-donation cardiovascular pathology	3	4%

1. Active smoking: 18; smoking quitted: 15.

of cases. Smoking and dyslipidaemia were noted in 44 and 29% of cases respectively. An absence of CVRF was noted in 8% of cases (5 RD and 1 CA). In the 58 CA-types CSARD, 7 had 1 CVRF; 2 or more CVRF were noted in 50 cases (86%), 3 or more in 38 cases (65%), 4 or more in 20 cases (34%), and 5 in 5 cases (9%). In the 5 CA that began before donation, without being screened at the PDI, donors had 2 or 3 CVRF. In the 17 RD-types CSARD, only 4 (23%) had 3 CVRF and none had 4 or 5. In 3/75 cases (4%), a history of CV disease not detected at the PDI would have contraindicated donation. In these 3 cases, the CSARD was a RD.

4. Discussion

4.1. Description of CSARD

This large retrospective study provides a more complete knowledge of CSARD likely to complicate blood and blood component donations, knowledge that was previously very fragmentary for CA [14,15], and to our knowledge never published for RD. For each of the two nosological entities concerned, CA and RD, it made it possible to specify the pathologies observed and the characteristics of the donors concerned. The main strength of this study comes from the haemovigilance database established since 2010 with the regulatory mandatory reporting of SARD in France [16]. The most severe SARD are regularly analysed by a permanent scientific committee of the National Agency for the Safety of Medicines and Health Products (ANSM). It is this committee that has taken up this concern to specifically study CSARD given their seriousness.

Common features of CA and RD type CSARD are a strong male predominance, a median age slightly higher than that of the

Table 5
Number of CVRF noted in donors in the CSARD studied.

	Total	0	1	2	3	4	5
MI	38	1	4	7	12	11	3
ACS	13	0	2	3	3	3	2
AP	7	0	1	2	3	1	0
Total CA	58	1	7 (12%)	12 (21%)	18 (31%)	15 (26%)	5 (9%)
RD	17	5	6	2	4	0	0
Total CSARD	75	6 (8%)	13 (17%)	14 (19%)	22 (29%)	15 (20%)	5 (7%)

standard donor population (except for women with RD), an overall low frequency, and above all a significantly higher frequency with AD compared to WBD. Age by gender constitutes the first universally recognized CVFR [10]. The incidences observed for CA and RD, respectively 1.65 and 0.48 / 10^6 donations, confirm that these are fortunately very rare SARD. To our knowledge, no published data allow us to compare these incidences with those of other countries or regions. Given the rarity of these SARD, only multinational studies based on superimposable reporting databases with large numbers of donors will be able to provide comparative data.

An increased incidence of coronary SARD with AD compared to WBD had been suspected a long time ago [14]. It had not been found in a multivariate analysis of adverse cardiovascular events (ACVE) reported in the French haemovigilance system in 2012 and 2013 [17]. But these were ACVE going far beyond the scope of CSARDs, with a study grouping together 15 CSARD and 27 vascular (non-cardiac) SARD, including 21 thrombotic or embolic accidents of venous origin. On the other hand, another study analysing French haemovigilance data from 2010 and 2011 had already noted a significantly higher frequency of MI after platelet AD vs. WBD, despite very small numbers [18]. In terms of possible mechanisms to explain this difference, donor platelets may be activated during the apheresis procedure and recirculate for 24 h or more after donation [19,20]. These platelet activations, associated with the donor's hemodynamic response to intermittent volume depletions [21], and a formation of platelet-neutrophil complexes [22], could explain, at least in part, the higher frequency of CA associated with AD compared with WBD. In any case, the confirmation of this result leads to recommend considering the AD as an additional risk factor. This difference between both types of donations was also found for the RD, and in the absence of available scientific evidence, it seems logical to consider, even provisionally, that the mechanisms cited above could be at least partly involved.

The severity observed is different between CA and RD CSARD. The first one are all severe, leading the donor to either hospitalisation (91%) or death (9%). RD CSARD are significantly less severe, with no need for hospitalisation in most cases, and no deaths in this group. Again, to our knowledge, no publication allows us to compare these data with those of other countries or regions.

4.2. CVRF and prevention

The CVRF search also differentiates between CA and RD CSARDs. In the first one, the presence of more than 3 CVRFs was noted in about 34% of donors, but in none of the second one. And the CSARD had started before the donation in 9% of the CA without this additional CVRF detected in the PDI. Given the severity of CA CSARD, these observations led us to consider the possibility of reducing their incidence by specifying the donor selection criteria (DSC) of prospective donors regarding CV risk. This seems all the more necessary as France, like many countries, has raised the age limit for blood donation, opening donation to older donors [23]. Other countries have even removed the upper age limit [24]. And older donors intend to continue as long as they are eligible [25].

In practice, a search for CVRF beyond the pre-donation questionnaire and BP measurement, with cholesterol and glycated haemoglobin (HbA1C) assays, even if it is likely to reveal abnormalities not detectable by PDI [26], is not feasible on a large scale. The SCORE tables for assessing the risk of a CV event at 10 years [9] are also not usable in the practice of PDI of prospective donors (PDs), because they imply having a recent total cholesterol result. Based on the observations of our study on CVRF, it seems relevant to propose to any PD with a CVRF (most often age/gender) to actively look for the 6 other CVRFs considered in this study and recent clinical symptoms of coronary pathology, during the PDI. From this information, the integration of CV risk when a PD has more than 3 CVRFs or recent suggestive clinical symptoms could lead to a permanent deferral, or a temporary deferral with return to donation provided the person positive advice of a cardiologist. This should particularly apply to AD, who are at higher risk than WBD prospective donors.

But today, faced with a concern for which scientific evidence is lacking, it seems prudent to rely on the approach described by TRANSPOSE [4] to evaluate the DSC. The approach simplified compared to that proposed by the Alliance of Blood Operators [27] includes the following steps. (i) Characterise the risk in general; (ii) Invite a group of international experts to the work; (iii) List options for mitigating the risks; (iv) List potential consequences, including impact on health economics, feasibility or costs, or impact on donor behaviour or return to donation; (v) Propose donor selection criteria (DSC); (vi) Invite stakeholders to comment. The decision should be based on full consensus. In practice, we wish to submit our proposal for DSC for CV risk to an international expert group (ex TRANPOSE, ISBT Donor Group), as a basis for discussion, which the data from our study should help to support. We are aware that, whatever the conclusion of the expert group, as already described, CA may always occur immediately following apheresis in donors without detectable CVRF [15]. For RD, the low number of CVRF observed does not allow to consider specific DSC.

4.3. Imputability

Strict application of the rules for determining imputability [6,28] should lead to excluding the imputability of most CSARD, "*when the evidence allows the adverse reaction to be attributed to other causes*". This is clearly the case for CA CSARD of atheromatous origin, the majority of studied cases. Furthermore, even if the scientific evidence is limited, it seemed relevant to extend the usual time limit for considering the imputability of a CSARD from 24 to 48 h. This extension had two consequences. First, it made it possible to retain the imputability of 20% of the CSARD studied, occurring between 24 and 48 h after the donation. By following the usual recommendations [1,6], the imputability of these 15 cases would not have been retained, in a manner probably poorly justified for many, given the arguments of troponin kinetics for MI [7,8]. On the other hand, this extension resulted in the exclusion of 39 CSARD that occurred after 48 h up to 6 days. The lack of scientific evidence to support our proposal to add an additional criterion to imputability, based on the aggravating (A) or triggering (T) role of the donation, with three levels based on chronology, is a weakness of the study. But in practice, the application of these levels to the cases of this study has shown that it was easy and greatly facilitated the evaluation of the role played by the donation in these CSARD.

4.4. Limitations

In addition to the limitations regarding imputability, cited above, this observational retrospective study cannot shed light on the causal links between donations and CSARD. Nor can it provide an answer to the question of the comparative incidence of serious adverse cardiac events in blood and blood component donors on the one hand, and in the general population on the other hand. In older studies, regular blood donation was found to be associated with a reduction in the frequency of MI compared to a control population of non-donors matched for gender and age [29,30]. Several studies appear to show a protective effect on cardiovascular morbidity and mortality of high-frequency blood donation in the long term, independently of the "healthy donor effect" related to repeated selection of regular donors [30–32]. A cohort study in more than 1,5 million Danish and Swedish donors

showed an association between elevated haemoglobin and risk of MI [33]. However, a recent review highlighted the methodological weakness of studies on this topic and concluded that a protective effect of blood donation against cardiovascular risk remains uncertain [34]. For these authors, the answer to this question would require either a controlled prospective study or the application of advanced statistical models to observational data, with sufficient numbers.

5. Conclusions

This descriptive study provides a better understanding of CSARD, which are rare but always severe when they are of the CA type. The CVRF observed in these SARD provide the basis for thinking about the relevance of changing donor selection criteria for CV risk, particularly for AD, which are more at risk than WBD. The approach described by TRANSPOSE for such a review [4] should be considered. Depending on their conclusions, a complementary study with large numbers of people should evaluate whether a more formalised consideration of CVRF in the PDI could reduce the frequency of CA-type CSARD.

Author contribution

Dr Boudjedir had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Folléa, Boudjedir, Carlier, Hervé, Mertes, Somme.

Acquisition, analysis, interpretation of data: Boudjedir, Folléa, Carlier, Hervé, Mertes, Somme, Lenzotti.

Drafting of the manuscript: Folléa, Boudjedir, Lenzotti.

Critical revision of the manuscript for important intellectual content: Folléa, Boudjedir, Lenzotti, Carlier, Hervé, Mertes, Somme,

Statistical analysis: Lenzotti, Folléa.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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