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PERIPROCEDURAL DYNAMICS OF BIOMARKERS OF MYOCARDIAL INJURY, SYSTEMIC INFLAMMATION AND THROMBOGENICITY AFTER PULMONARY VEIN ISOLATION FOR ATRIAL FIBRILLATION USING CRYOGENIC AND PULSED FIELD ENERGY

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ПЕРИПРОЦЕДУРНА ДИНАМИКА НА БИОМАРКЕРИТЕ ЗА МИОКАРДНА УВРЕДА, СИСТЕМНО ВЪЗПАЛЕНИЕ И ТРОМБОГЕННОСТ СЛЕД ИЗОЛАЦИЯ НА БЕЛОДРОБНИТЕ ВЕНИ ЗА ПРЕДСЪРДНО МЪЖДЕНЕ ЧРЕЗ КРИОГЕННА И ПУЛСОВА ЕНЕРГИЯ

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Abstract.

Introduction: Pulmonary vein isolation (PVI) for atrial fibrillation (AF) induces myocardial necrosis. The extent of myocardial injury and systemic inflammatory or thrombotic response may vary depending on the ablation energy modality. It is not known whether the maximum diameter of 'single shot" ablation catheters influences the magnitude of biomarker release. We aimed to study the temporal profiles of cardiac (high-sensitivity cardiac troponin I, hs-cTn), inflammatory (C-reactive protein, CRP), and thrombotic (D-dimer) biomarkers, as well as creatinine, within 24 hours of PVI, using cryogenic (CBA) or pulsed field energy (PFA). **Materials and methods:** We prospectively studied consecutive patients with non-permanent AF undergoing first-time PVI by CBA or PFA. Data were collected on the demographic and clinical characteristics, echocardiographic and procedural parameters, and biomarker levels. Blood samples were collected pre-procedure, 6-8 hours post-procedure, and 20-22 hours post-procedure. Repeated measures ANOVA was used for longitudinal comparisons after log-transformation where required; between-group differences were assessed using the Brunner-Munzel test or the chi-square test. A P-value < 0.05 was considered statistically significant. **Results:** Each group comprised 35 patients with no significant differences in demographic, clinical, or echocardiographic characteristics. Procedure duration was longer with CBA (90 vs 70 min., p < 0.001). hs-cTn increased in both groups, with a higher peak (10217 ng/L vs 5831 ng/L, p = 0.034) and more rapid decline (6431 ng/L vs 4947 ng/L, p = 0.078) in the PFA group. CRP was higher after CBA (11.7 mg/L vs 4.5 mg/L, p < 0.001). D-dimer and creatinine did not change significantly. Biomarker changes were dependent on the time of sample collection and energy modality used, but not on the diameter of the ablation catheter. **Conclusion:** Compared to CBA, PFA is associated with a substantially greater early increase of hs-cTn within the first few hours, followed by a steeper decline by the following day. CRP increases more after CBA, while D-dimer and creatinine are not affected by either ablation modality.

Key words: high-sensitivity cardiac troponin; C-reactive protein; D-dimer; atrial fibrillation; pulsed field ablation; cryoablation.

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Резюме.

Въведение: Изолацията на белодробните вени (ИБВ) за предсърдно мъждене (ПМ) предизвиква миокардна некроза. Миокардното увреждане и системният възпалителен или тромботичен отговор може да варират в зависимост от вида на аблационната енергия. Не е ясно дали максималният диаметър на аблационен катетър тип "single shot" повлиява големината на биомаркерното освобождаване. Целта ни беше да проучим времевия профил на сърдечни (високосензитивен тропонин I, hs-cTn), възпалителни (С-реактивен протеин, CRP) и тромбо-

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тични (D-димер) биомаркери, както и на креатинин, в рамките на 24 часа след ИБВ с криогенна (CBA) или пулсова (PFA) енергия. **Материал и методи:** Проучихме проспективно последователни пациенти с неперманентно ПМ и първа ИБВ чрез CBA или PFA. Бяха събирани данни за демографските и клинични характеристики, ехокардиографски и процедурни параметри, и биомаркерни нива. Кръвни проби бяха вземани преди процедурата, 6-8 часа след нея, и 20-22 часа след нея. Лонгитудиналните сравнения бяха направени чрез repeated measures ANOVA (след логаритмична трансформация при необходимост), а междугруповите разлики бяха оценени чрез тест на Brunner-Munzel и тест χ^2. Стойност на $P < 0.05$ беше приета за статистически значима. **Резултати:** Във всяка група бяха включени по 35 пациенти, без значими разлики в демографските, клиничните и ехокардиографските характеристики. Процедурната продължителност беше по-голяма при CBA (90 с/у 70 мин., $p < 0.001$). hs-cTn се увеличи в двете групи, с по-голям пик (10217 ng/L с/у 5831 ng/L, $p = 0.034$) и по-бърз спад (6431 ng/L с/у 4947 ng/L, $p = 0.078$) след PFA. CRP беше по-висок след CBA (11.7 mg/L с/у 4.5 mg/L, $p < 0.001$). D-димерът и креатининът не се промениха значимо. Промените в биомаркерите се оказаха зависими от времето на вземане на пробите и от използваната енергия, но не и от диаметъра на аблационния катетър. **Заключение:** В сравнение с CBA, PFA е свързана с много по-голямо увеличение на hs-cTn в първите часове след аблацията, последвано от по-стръмен спад на следващия ден. CRP се увеличава повече след CBA, докато D-димерът и креатининът не се повлияват от вида на аблацията.

Ключови думи: високочувствителен сърдечен тропонин; С-реактивен протеин; D-димер; предсърдно мъждене; пулсова аблация; криоаблация

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Introduction

Pulmonary vein isolation (PVI) is the cornerstone in the management of symptomatic atrial fibrillation (AF). Irrespective of the ablation energy used, it induces myocardial necrosis surrounded by oedema and aseptic inflammation in the adjacent tissue, later on replaced by fibrotic scar, thereby creating lines of permanent conduction block around the PV ostia. The extent of myocardial injury and the systemic inflammatory or thrombotic response may vary depending on the ablation energy modality [1-3]. High-sensitivity cardiac troponins (hs-cTn) are established markers of myocardial injury, while D-dimer reflects thrombogenesis, and C-reactive protein (CRP) indicates systemic inflammation. Serum creatinine may capture procedure-related renal effects and influence the post-procedural levels of other biomarkers. Although cardiac biomarker release following ablation is well documented, comparative biomarker kinetics across different energy sources have been relatively poorly studied [1, 2]. Furthermore, it is not known whether the maximum diameter of “single shot” ablation catheters, potentially resulting in a larger footprint, influences the magnitude of biomarker release.

Our aim was to characterize and compare the temporal profiles of hs-cTn, CRP, and D-dimer, as well as creatinine, within 24 hours of PVI for AF, using cryogenic or pulsed field energy, and to compare within-group changes over time and between-group differences in temporal dynamics.

Materials and methods

Patient population

This is an investigator-initiated, single-center, prospective, observational cohort study of consecutive patients with AF undergoing their first PVI procedure, performed between May 2025 and January 2026. The inclusion criteria were the following: patients with symptomatic paroxysmal or persistent AF, refractory to at least one antiarrhythmic drug, undergoing first-time PVI by means of cryogenic or pulsed field energy. The exclusion criteria were: prior PVI procedure; delivery of additional linear and/or focal lesions outside the PV ostia during the procedure; active infection or inflammatory disease; non-adherence to anticoagulation therapy. The study protocol followed standardized procedures across groups (same procedural workflow, anticoagulation, timing of blood draws, and laboratory assay kits) and was approved by the local ethics committee. All patients signed written informed consent.

Power analysis with regard to hs-cTn showed that the minimum required sample size was 62, to achieve a power of 0.9, assuming an effect size $\eta^2_p = 0.15$ and type I error set to 0.05.

All patients underwent preprocedural transthoracic echocardiography for assessment of the left atrial (LA) anteroposterior diameter in the parasternal long axis view, LA volume, LA volume index, left ventricular ejection fraction, presence of structural heart disease, and valvular abnormalities. All patients underwent con-

trast-enhanced multidetector computed tomography scan of the left atrium. The image series were segmented, and three-dimensional reconstructions of the left atrium and the PVs were generated prior to the procedure. These reconstructions were used during the procedure, but did not influence the choice of ablation modality. The procedures were scheduled consecutively by order of inclusion of the patients in the study. Due to logistical constraints PFA procedures were performed monthly in two or three consecutive days (the PFA console was used by several centers on a monthly schedule). Oral anticoagulation was not interrupted, and a bolus of 100 U/kg unfractionated heparin was administered immediately after the transseptal puncture and thereafter during the procedure as necessary.

Pulmonary vein isolation

All ablations were performed by two operators experienced in radiofrequency (RF) point-by-point PVI and cryoballoon PVI. The PFA group included patients since the inception of this modality in the hospital. Intracardiac echography was not used.

Cryoballoon ablation (CBA) was performed using a technique, described previously [4], with the Smart-Freeze cryoconsole (Boston Scientific, MA, USA). Briefly, two steerable diagnostic catheters were inserted: 10-polar catheter in the coronary sinus and 4-polar catheter over the His bundle. Single transseptal puncture was performed and a long non-steerable SL0 introducer (Abbott, MN, USA) was placed in the LA. It was exchanged over a wire for a 12.7F steerable introducer for cryoablation. The last eight transseptal punctures were done directly through the steerable introducer, thus obviating the need for introducer exchange. An 11.8F cryoballoon with fixed (POLARx, 28 mm) or variable (POLARx FIT, 28-31 mm) diameter was introduced into the left atrium over a 3.3F 8-polar circular mapping catheter with 6 mm interelectrode distance. The inflated cryoballoon was advanced into each PV until occlusion was achieved as verified by a contrast injection. Freezing time was 240 seconds for each of the left-sided PVs and 180 seconds for each of the right-sided PVs. Delivery of additional freezes was left on the discretion of the operator. The freezing sequence always commenced with the left superior PV, followed by the left inferior, right inferior and right superior PV. High-output pacing was delivered in the superior caval vein to monitor the function of the right phrenic nerve during cryoablation of the right-sided PVs. Electrical isolation of all PVs was verified by the disappearance or dissociation of the PV potentials on the circular mapping catheter positioned in each vein.

Pulsed field ablation (PFA) was performed using the Farapulse console (Boston Scientific, MA, USA) under deep sedation with midazolam, fentanyl and propofol, administered by an anesthesiologist. The same diagnostic catheters were deployed as described above. Transseptal access was achieved via the SL0 introducer, which was then exchanged for a 13F steerable introducer. The last 10 transseptal punctures were done directly using the steerable sheath. Once LA access was established, a 12F pentaspline PFA catheter (Farawave, 31 or 35 mm) was advanced over a guidewire into each PV. Catheter position was assessed by fluoroscopy. The ablation commenced with the left-sided PVs. The catheter was deployed in each PV ostium in “basket” and “flower” configuration, and a minimum of eight pulses per vein were delivered at 2 kV in asynchronous mode. Two anchoring pulses were delivered at the anterior part of each PV carina. Delivery of additional PFA pulses was left on the discretion of the operator. Electrical isolation of the PVs was verified by the abolition of the PV potentials on the pentaspline catheter.

The catheters and sheaths were removed immediately upon completion of the procedure, and hemostasis was achieved by placing Z-sutures at the access sites, followed by bed rest for 5 hours. Protamine was not administered at the end of the procedure.

Data collection and laboratory analysis

Data were collected on the demographic and clinical characteristics of the patients, comorbidities, echocardiographic parameters, procedure duration (skin-to-skin time), and dose-area product (DAP). Blood samples for biomarker analysis were collected at prespecified time points: pre-procedure at hospital admission – T0 (baseline); 6-8 hours post-procedure – T1; and 20-22 hours post-procedure – T2 (the morning after the procedure, prior to discharge). Biomarkers measured were: high-sensitivity cardiac troponin I (hs-cTn) at T0, T1, and T2; D-dimer at T0, T1, and T2; CRP at T0 and T2; and serum creatinine at T0 and T2.

All measurements were done in the hospital laboratory. Cardiac troponin was measured by immunochemiluminescent assay on an ARCHITECTi analyzer, with an upper limit of the normal range (ULN) of 14.3 ng/L for women and 34.5 ng/L for men; D-dimer was measured by turbidimetric assay on an Innovance CS 2500i Sysmex analyzer, with a ULN of 0.55 mg/L; CRP was measured by immunoturbidimetric assay on an Olympus 480 analyzer, with a ULN of 5 mg/L.

Statistical analysis

The statistical analysis was performed using *jamovi* v.2.7 (The jamovi project 2025) [5, 6]. Data distribution was assessed by the Shapiro-Wilk test, and homogeneity of variances – by the Levene’s test. Continuous data are presented as median (25th – 75th percentile)

or mean ± standard deviation. Proportions are presented as percentages. Repeated measures ANOVA was used for longitudinal comparisons of continuous variables across groups. Log transformation of biomarker data with non-normal distribution was performed before running the repeated measures ANOVA, with Greenhouse-Geisser sphericity correction applied as necessary. Between-group differences were assessed by the Brunner-Munzel test or the chi-square test for association. A P-value < 0.05 was considered statistically significant.

Results

Seventy patients (40 men) satisfied all inclusion and exclusion criteria during the study period and were enrolled in the analysis. The patients were distributed equally between the two groups (CBA and PFA). Baseline characteristics are presented in Table 1; no significant differences were observed between groups.

Procedural characteristics are summarized in Table 2. Total procedure duration was significantly shorter in the PFA group. In the cryo group larger size balloon was used much more frequently than the larger size pentaspline catheter in the PFA group. In the cryo group there were one transient phrenic palsy and one inguinal hematoma, while in the PFA group there was one inguinal hematoma. Both patients with vascular access site complications were treated conservatively without prolongation of the hospital stay.

Table 2. Procedural characteristics of the patients by ablation energy

	Cryo (n = 35)	PFA (n = 35)	p
Number of energy applications	5 (4-6)	36 (36-40)	N/A
Ablation time (sec)	990 (840-1115)	--	N/A
Left atrial dwell time (min)	44 (40.5-51.5)	na	N/A
TTECV done, n (%)	11 (15.7)	8 (11.4)	0.42
Total duration (skin-to-skin) (min)	90 (80-97.5)	70 (60-85)	**< 0.001**
DAP (mcGy*m^2)	3339 (2425-5158)	3451 (2350-4415)	0.776
Fluoroscopic time (min)	17 (13.5-20.5)	15 (13.3-19)	0.347
Large diameter balloon/PFA catheter, n (%)	18 (25.7)	6 (8.6)	**0.003**

The central tendency is presented by median (25th-75th percentile). Proportions are presented as percentage of the entire study population. TTECV – transthoracic electrical cardioversion; DAP – dose-area product; N/A – not applicable; na – not available.

The biomarker dynamics over time and changes from baseline within both groups are shown in Table 3 and Figure 1. There was significant, albeit small and clinically irrelevant, difference in baseline hs-cTn levels between groups. Nevertheless, baseline hs-cTn values were entirely within the normal range in both groups.

The results of the repeated measures ANOVA analysis of longitudinal biomarker changes are summarized in Tables 4 and 5. Between-subject factor was ablation energy. Larger diameter of cryoballoon/PFA catheter was used as a covariate. Log transformation was done for biomarkers data, thus allowing for the assumptions of the repeated measures ANOVA to be met. Greenhouse-Geisser correction was also used as necessary.

Table 1. Characteristics of the patients by ablation energy used

	Cryo (n = 35)	PFA (n = 35)	p
Sex, n M:F (% M:F)	18 : 17 (25.7 : 24.3)	22 : 13 (31.4 : 18.6)	0.334
Age (years)	61.4 ± 10.3	62.5 ± 9.67	0.728
BMI (kg/m2)	28.3 (26.2 – 32.7)	28.7 (25.9 – 31.2)	0.927
Obesity (%)	17.1	20	0.621
Arterial hypertension (%)	38.6	40	0.771
Diabetes mellitus (%)	14.3	11.4	0.584
Coronary artery disease (%)	2.9	1.4	0.555
HFrEF (%)	10	5.7	0.324
HFpEF (%)	11.4	12.9	0.78
LVEF (%)	56 (50 – 61)	56 (54.5 – 61)	0.315
LAD (mm)	42 (39 – 45)	43.5 (38 – 46.5)	0.387
LAV (ml)	88.2 (73 – 117)	88 (65.6 – 115)	0.727
LAVI (ml/m^2)	42 (35 – 51.2)	42.8 (35.7 – 55.3)	0.861
eGFR (ml/min/1.73 m^2)	74.4 ± 18.8	74.5 ± 21.4	0.968

The central tendency is presented by median (25th – 75th percentile), or mean ± standard deviation. Proportions are presented as percentage of the entire study population. Obesity was defined as BMI ≥30. Coronary artery disease was defined as prior myocardial infarction and/or percutaneous coronary intervention and/or coronary artery bypass surgery. BMI – body mass index; HFrEF/HFpEF – heart failure with reduced/preserved ejection fraction; LVEF – left ventricular ejection fraction; LAD – left atrial anteroposterior diameter; LAV – left atrial volume; LAVI – left atrial volume index; eGFR – estimated glomerular filtration rate.

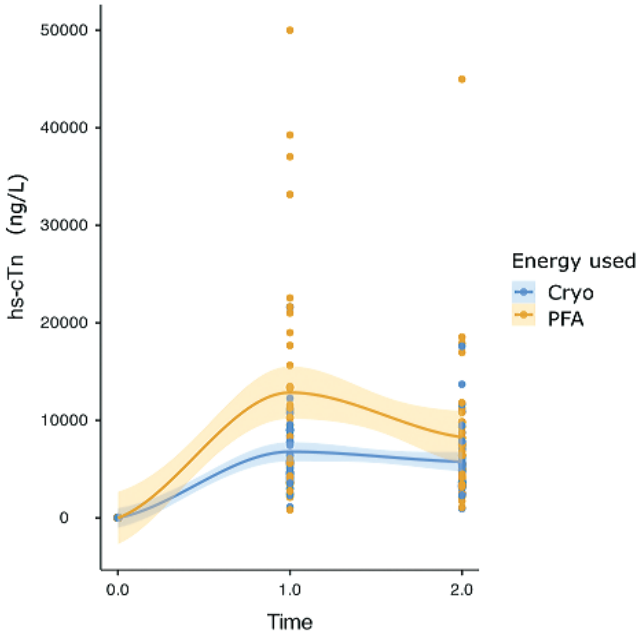

Fig. 1. Scatter plot illustrating the temporal dynamics of hs-cTn levels with 95% confidence intervals at the three measurement time points (T0, T1, T2). The CBA group is shown in blue, the PFA group – in ochre

Table 3. Biomarker levels and changes from baseline in both groups

	Cryo (n = 35)	PFA (n = 35)	p
Creatinine T0 (mcmol/L)	91.8 ± 18.5	94.4 ± 20.4	0.633
Creatinine T2 (mcmol/L)	89 (80-100)	90 (78-107)	0.751
Creatinine ΔT2-T0 (mcmol/L)	-2 (-9 ÷ +3)	-2 (-9 ÷ +8)	0.345
hs-cTn T0 (ng/L)	2.7 (1.6-6.3)	1.5 (0.75-2.95)	**0.006**
hs-cTn T1 (ng/L)	5831 (4283-8966)	10217 (4517-16662)	**0.034**
hs-cTn T2 (ng/L)	4947 (3330-7237)	6431 (4209-9575)	0.078
hs-cTn ΔT1-T0 (ng/L)	5829 (4280-8963)	10216 (4516-16662)	**0.034**
hs-cTn ΔT2-T0 (ng/L)	4947 (3326-7236)	6428 (4199-9574)	0.08
CRP T0 (mg/L)	2.8 (1.45-5.45)	1.5 (0.8-3.55)	0.076
CRP T2 (mg/L)	11.7 (5.9-15.7)	4.5 (2.4-8.35)	**< 0.001**
CRP ΔT2-T0 (mg/L)	7.8 (3.8-11)	2.6 (0.9-5.6)	**< 0.001**
D-dimer T0 (mg/L)	0.19 (0.19-0.19)	0.19 (0.19-0.26)	0.328
D-dimer T1 (mg/L)	0.25 (0.19-0.42)	0.25 (0.19-0.37)	0.397
D-dimer T2 (mg/L)	0.23 (0.19-0.34)	0.22 (0.19-0.358)	0.782
D-dimer ΔT1-T0 (mg/L)	0.04 (0-0.19)	0.005 (0-0.147)	0.115
D-dimer ΔT2-T0 (mg/L)	0.01 (0-0 .09)	0.00 (0-0.06)	0.376

Δ – difference between two timepoints.

Table 4. Log-transformed longitudinal biomarker changes within the groups

Biomarker	Effect	Correction	GG ε	df (num)	df (den)	F	p	η^2_p
hs-cTn	Time	GG	0.552	1.1	73.92	109.05	**< 0.001**	0.619
hs-cTn	Time x Energy used	GG	0.552	1.1	73.92	4.76	**0.029**	0.066
hs-cTn	Time x Larger catheter size	GG	0.552	1.1	73.92	2.29	0.132	0.033
D-dimer	Time	GG	0.777	1.55	97.91	0.0351	0.935	0.001
D-dimer	Time x Energy used	GG	0.777	1.55	97.91	2.2857	0.119	0.035
D-dimer	Time x Larger catheter size	GG	0.777	1.55	97.91	1.3791	0.254	0.021
CRP	Time	none	1	1	67	3.24	0.077	0.046
CRP	Time x Energy used	none	1	1	67	7.42	**0.008**	0.1
CRP	Time x Larger catheter size	none	1	1	67	1.71	0.195	0.025

GG – Greenhouse-Geisser correction. Degrees of freedom were adjusted using Greenhouse–Geisser correction when Mauchly's test indicated violation of the sphericity assumption. η^2_p represents partial eta squared as a measure of the effect size.

Table 5. Log-transformed longitudinal biomarker changes between the groups

Biomarker	Effect	df (num)	df (den)	F	p	η^2_p
hs-cTn	Energy used	1	67	0.0613	0.805	0.001
hs-cTn	Larger catheter size	1	67	0.6066	0.439	0.009
D-dimer	Energy used	1	63	0.113	0.738	0.002
D-dimer	Larger catheter size	1	63	3.661	0.060	0.055
CRP	Energy used	1	67	7.107	**0.01**	0.096
CRP	Larger catheter size	1	67	0.593	0.444	0.009

Abbreviations and symbols are as indicated in Table 4.

Discussion

The main finding of this prospective, single-center study is that both CBA and PFA are associated with substantial release of hs-cTn following a first PVI procedure for AF, but the magnitude of the early increase is significantly greater with PFA. CRP also increased in both groups over the short term, although this increase did not reach statistical significance in the within-group analysis. However, a significant between-group difference was observed, with a markedly greater CRP increase in the CBA group. D-dimer dynamics did not show any dependence on time and energy modality. Notably, hs-cTn, CRP and D-dimer release did not seem to be influenced by the use of larger size ablation catheters.

Several possible explanations exist for the observed differences in troponin levels. One could assume that the ablated area in PFA is larger than in CBA, owing to the broader footprint of the pentaspline catheter, particularly in its flower configuration, allowing for more extensive antral ablation [7]. On the other hand, Kawamura et al. performed high-density mapping 75 days after an index PVI procedure with PFA (Farapulse), CBA (Arctic Front), RF and laser balloon ablation, and found no statistically significant difference between ablation modalities in terms of cumulative LA ablation area [8]. However, as PFA is less influenced by blood flow velocity, catheter orientation and tissue contact, it may result in a more efficient and transmural lesion.

Another observation in our study is that PFA is associated with a higher peak of cardiac troponin and a more rapid decline by the following day. This could be attributed to the well-recognized tissue selectivity and limited collateral damage of PFA. Indeed, irreversible electroporation occurs when a certain threshold is exceeded, which varies vastly between different tissues. For example, said threshold is 750 V/cm for human cardiomyocytes and 1750 V/cm for vascular smooth muscle cells or endothelium [9, 10]. If the microcirculation is spared in PFA, this may result in a "wash-out" phenomenon characterized by an early peak and rapid decline, which is consistent with our findings. This is in stark contrast to the diffuse and nonspecific hemorrhage, as well as coagulation necrosis resulting from osmotic injury and intracellular ice formation, seen in CBA [11].

We found no difference in the values of troponin in the subgroups treated with the larger-sized catheters or balloons. The diameter of the POLARx FIT cryoballoon can be adjusted, but the larger diameter was not applied by default for every vein, instead only when occlusion was deemed unsatisfactory by the operator with the smaller diameter. This, along with the fact that we do not have the exact number of applications, using the larger diameter, does not allow us to draw any firm conclusion on its effect on troponin levels. A recent study showed that the total posterior scar area was significantly larger when using the 31 mm diameter of the POLARx FIT cryoballoon, however the difference was only 2.8 mm^2 [12]. Whether this difference is large enough to produce any detectable effect on the troponin levels compared to CBA with a 28 mm cryoballoon is not known. The rationale for using a larger (35 mm) PFA catheter is based on CT and echocardiographic evidence of extraordinary large pulmonary venous ostial or left atrial dimensions, or various pulmonary venous variants such as common ostia or acute take-off angles. These factors present a more complex technical challenge pertaining to catheter positioning, stability and finally lesion formation. All of the aforementioned, combined with the small subgroup size (6 of 35 patients), make the absence of a detectable effect of the larger pentaspline catheter on post-procedural troponin levels less reliable and this result should be interpreted with caution.

The goal of RF ablation is the creation of a circumferential line, measuring just a few millimeters in width around the PVs. This differs from the pentaspline catheter, which inherently targets a substantially broader area than point-by-point lesions, leading to a much larger number of injured cardiomyocytes. Several studies have already outlined the differences in the temporal kinetics of troponin release after PFA and compared them to RF ablation. The troponin increase seems to be consistently higher with PFA, depending on the used troponin assay [1, 3, 13-15].

Despite the significantly shorter procedural duration in the PFA group, the dose-area product was similar between groups. The former is expected, considering the fact that PFA is technically simpler to execute with a shallower learning curve and the application duration is much shorter. Of course, this does not obviate the need for fluoroscopy, in the absence of intracardiac echography, to initially position the catheter in the vein, switch between configurations, as well as ensure a circumferential lesion by rotating the catheter as per

manufacturer guidelines. The same applies to the various maneuvers described in CBA, e.g. “hockey stick”, “pull-down” and “big loop”, resulting in a comparable DAP and fluoroscopy time between the two modalities.

The dominant mechanism of cardiomyocyte death in irreversible electroporation is apoptosis [16]. Pre-clinical histopathological studies have shown that both PFA and CBA lesions consist of organized and homogenous fibrosis with well-demarcated boundaries [17, 18]. Nevertheless, in our study CRP increased significantly more in the CBA group, despite the much smaller enzyme release. Due to this discrepancy, also observed in other studies, some have hypothesized that systemic inflammation is a manifestation of collateral damage, e.g. silent lesions in the esophagus, nerves or pericardium [19]. As was mentioned earlier, PFA limits unintentional damage to adjacent tissues, resulting in a milder inflammatory response.

Serum creatinine showed insignificant intra- and inter-group dynamic. While patients in both groups received a large volume of i.v. fluids, intraprocedural hydration was larger in the PFA group owing to the added perfusion of the ablation catheter itself and of the steerable sheath. The risk of renal injury depends on the number of PFA applications. It has been established that some degree of hemolysis occurs in nearly 95% of patients receiving more than 60 PFA applications [20], with some studies reporting a significant rise in creatinine, even meeting acute kidney injury criteria, up to 48 hours after ablation [21]. This, coupled with the fact that the number of applications in our study did not exceed 46, likely accounts for the absence of significant creatinine change. CBA tends to either have no effect on creatinine levels, or lead to a slight decrease [21, 22].

D-dimer was not influenced by either ablation modality. Several studies exploring the thrombogenicity by the dynamics of coagulation parameters and indirectly by assessing endothelial injury have not shown that PFA is associated with an increased thromboembolic risk [23]. Importantly, PFA significantly shortens left atrial dwell and ablation times, which may further reduce thrombogenic risk. In contrast to our findings, CBA has been shown to exert a pro-coagulant response [24, 25].

Limitations

This is a non-randomized observational study without external funding, which significantly shortened the follow up and limited the available resources for laboratory testing outside the necessary hospital stay. This inhibited our ability to precisely characterize the temporal dynamics of the studied biomarkers, especially for CRP, which tends to peak at 24-72 hours post injury. Importantly, CRP and creatinine were not assessed at the intermediate time point which confounds their comparison to the other biomarkers. Other limitations include the small sample size and lack of long-term follow up, which does not allow for correlation with clinical outcomes based on the described laboratory values. Our data, regarding the biomarker dynamics with the different catheter diameters, should be interpreted with caution, if at all, owing to the very limited sample size and inherent differences between the two ablation modalities. Due to logistical reasons PFA procedures were performed monthly in two or three consecutive days. This may have introduced some bias and may explain the significant, albeit small and clinically negligible, difference of baseline hs-cTn.

Conclusion

Compared to CBA, PFA is associated with a substantially greater early increase of high-sensitivity cardiac troponin within the first few hours post-procedure, followed by a steeper decline by the next day. C-reactive protein increases more after CBA, while D-dimer and creatinine remain unaffected by either ablation modality when a standard number of energy application is used.

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