Aims
Thrombo-embolic events are one of the most feared complications related to atrial fibrillation (AF) ablation. Since radiofrequency (RF) energy is thought to be associated with a higher risk of thrombus formation than cryoenergy, the purpose of this study was to assess if the degree of activation of coagulation and inflammatory markers differed between ablation procedures performed with a cryoballoon catheter vs. a RF energy-based pulmonary vein ablation catheter (PVAC), respectively.

Methods and results
Thirty patients referred for AF ablation were randomized to pulmonary vein isolation with either the cryoballoon or the PVAC. Biomarkers were studied for endothelial damage (von Willebrand factor antigen), platelet activation (soluble P-selectin), and coagulation activity [prothrombin fragment 1 + 2 (F1 + 2) and D-dimer] at five different time points during the procedure. Troponin I (Trop I) and C-reactive protein were analysed to reflect myocardial destruction and inflammatory activity. Markers of endothelial damage and platelet activation increased after ablation in both the cryo and the RF group. Similarly, the D-dimer levels increased significantly \((P = 0.001)\) in both groups, whereas the F1 + 2 levels increased after the transseptal puncture only \((P = 0.001)\). The overall activation of the coagulation system was, however, comparable between the groups. The cryoballoon was associated with higher Trop I compared with the PVAC \((P < 0.001)\), but the ratios between biomarkers and Trop I were higher with the PVAC than with the cryoballoon.

Conclusion
Even though the cryoballoon causes a higher degree of myocardial destruction than the PVAC, markers of coagulation, endothelial damage, and inflammation were comparable between the two techniques.

Keywords
Atrial fibrillation • Catheter ablation • Coagulation • Cryoballoon • PVAC

Introduction
Thrombo-embolic events are uncommon but one of the most feared complications of atrial fibrillation (AF) ablation. Even though it is rare, occurring in about 0.3–1.5%,\(^1\)\(^–\)\(^3\) it may have severe consequences and every attempt should therefore be made to avoid it. Although radiofrequency (RF) energy has been the far more dominant energy source used for AF ablation, there is still no consensus on which form of energy should be used for pulmonary vein isolation (PVI). Previous animal studies have shown a higher rate of thrombus formation on the endocardial surface after RF ablation than after cryoablation.\(^7\) Activation of
What’s new?

- This is the first study exploring if there is any difference between the cryoballoon and the radiofrequency-based circular ablation catheter [pulmonary vein ablation catheter (PVAC)] with regard to the activation of biomarkers reflecting coagulation activity, endothelial damage, and platelet activation, in relation to the degree of myocardial damage and inflammatory activity.
- The observation that markers of coagulation, endothelial damage, and inflammatory response seems to be comparable between the two groups is an important contribution to the understanding of the mechanism of the reported higher-frequency of silent emboli with the PVAC compared with the cryoballoon.

Methods

Patients

The study population consisted of 30 patients referred for a first-time ablation of paroxysmal or persistent AF. Patients who were on treatment with acetylsalicylic acid or who were given vitamin K were excluded. Patients were randomized to PVI with either the cryoballoon catheter (Arctic Front, Medtronic) or with PVAC (Ablation Frontiers, Medtronic) using RF and the cryoballoon, specifically designed as ‘one-shot-tools’ for PVI, it was of great importance to clarify if the previously observed higher incidence of thrombus formation with RF energy could be translated into a difference in coagulation and/or inflammatory activity response. We hypothesized that RF ablation would result in a higher coagulation and inflammatory activity than cryoablation. The present prospective, randomized study, seems now even more important after reports of a larger risk for new silent cerebral embolism with the use of PVAC than with the use of the cryoballoon and the RF-irrigated tip ablation catheter.

Ablation procedure

The ablation procedure was standardized and performed with the patient awake, pre-medicated with diazepam and receiving ketobemide as analgetics during the procedure. A 5 French (F) bipolar catheter was positioned in the right ventricular apex for backup pacing and a 5 or 6F decapolar catheter was placed in the coronary sinus (CS). The transseptal puncture was performed with a Brockenbrough needle (St Jude Medical) guided by bi-plane fluoroscopy and intracardiac pressures. The 8F transseptal sheath (SL0, St Jude Medical) was then exchanged for a steerable 12 or 10F sheath (FlexCath, Medtronic), respectively, for the cryoballoon catheter and the PVAC. All introducers were continuously perfused with heparinized saline 5 U/mL.

Pulmonary vein entrance block was confirmed after ablation with a 10- or 20-polar circular mapping catheter during sinus rhythm for the right pulmonary veins (PVs) and during CS pacing for the left PVs. If the patient was in AF, conversion to sinus rhythm was obtained by either direct current (DC) cardioversion or by the use of ibutilide intravenously. The procedure time was defined as the time from application of local anaesthetics to the withdrawal of all catheters, the ablation time as the time from the first to the last application given. The duration of energy delivery was given by the generators. An electrophysiologist who was experienced with both catheter types performed all ablation procedures.

The cryoablation procedure was performed with a 10.5F cryoballoon catheter that delivers cryoenergy to the tissue by nitrous oxide (N2O). The 28 mm cryoballoon was chosen primarily unless the PV diameters were small and judged more suitable for the 23 mm balloon. A contrast medium (ioxaglate, Hexabrix©; 160 mg/mL) was injected distally to the balloon to visualize occlusion. Every attempt was made to achieve complete occlusion with the cryoballoon. Two applications of 5 min duration were given for every PV before conduc tion block was evaluated. If PV potentials were still present, 1–2 extra cryoballoon applications were delivered to that vein. In cases where PVI was not achieved after additional applications with the balloon or if an acceptable occlusion or position could not be achieved with the balloon catheter, a conventional 9F, quadripolar cryoablation catheter (Freezer Max, Medtronic) was used until complete PV isolation was achieved.

The RF ablation procedure was performed with the PVAC, a 9F, decapolar, circular catheter with phased RF energy that can be delivered simultaneously through one up to five electrode pairs, independently selectable. Different ratios of bipolar and unipolar energy, 4 : 1 or 2 : 1, may be chosen by the operator. The energy delivery is controlled by a software algorithm that modulates power to reach the target temperature (60°C), but always limits power to a maximum of 10 W per electrode. The PVAC was carefully positioned in the antrum of the PVs under fluoroscopic guidance. The RF energy was delivered for 60 s per application to electrodes in good contact with the tissue. Electrode pairs were deselected if the temperature did not reach more than 50°C. In case PV isolation was not achieved, a 7F decapolar, 4 mm tip RF ablation catheter (Celcius, Biosense Webster) was used for touch ups.
Blood sampling and laboratory methods for analysis

Von Willebrand factor (vWF) antigen and soluble (s) P-selectin were used as markers of endothelial damage and platelet activation, respectively. Coagulation activity was reflected by prothrombin fragment 1 + 2, a marker of thrombin generation, the central part of the coagulation and D-dimer, which reflects the fibrin turn-over, one of the final stages of coagulation. Blood samples for the coagulation biomarkers were collected at five different pre-specified time points during the procedure; from a peripheral vein (cubital vein) after insertion of the first introducer in the femoral vein (v baseline), from the left atrium (LA) after transseptal puncture but before heparin was administered (LA baseline), from LA before the start of ablation (LA pre-ablation), from LA when ablation was completed (LA post-ablation), and from the peripheral vein before the withdrawal of introducers (v post-ablation). Blood was drawn into vacutainer tubes containing 3.8% citrate. The first 10 mL of blood was discarded before sample collection. The samples were immediately centrifuged and frozen at −70°C until analysis.

For the detection of vWF antigen and D-dimer, STA-Liatest®vWF and Asserachrom® D-DI (Stago) were used. Soluble P-selectin was evaluated with enzyme-linked immunosorbent assay (ELISA) (R&D systems). Prothrombin fragment 1 + 2 was evaluated with ELISA (Enzygnost® F1 + 2) (Siemens). The interassay coefficients of variance were 4.4, 5.6, 9.9, and 11.2% for vWF antigen, D-dimer, sP-selectin, and F1 + 2, respectively. Troponin I (Trop I) was taken as a measure of myocardial destruction prior to, 6 and 24 h after the procedure and analysed using the Abbott Architect system. Levels <0.04 μg/L were considered as normal. The degree of inflammation was assessed by C-reactive protein (CRP) prior to and 24 h after the procedure. The endothelial damage and platelet activation was also analysed in relation to cardiomyocyte destruction and thus calculated as quotients between the vWF antigen and Trop I and between sP-selectin and Trop I. The coagulation activity in relation to cardiomyocyte destruction was calculated as the quotient between D-dimer and Trop I. The local ethic committee gave approval of the study protocol that complies with the Declaration of Helsinki and all patients gave written informed consent to be enrolled.

Statistical analysis

Continuous variables were given as mean and standard deviation (SD) or as median and interquartile range (25th–75th) as appropriate. Normally distributed variables were compared by Student’s t-test. For variables not normally distributed, Wilcoxon signed rank test was used for within-group comparison and Mann–Whitney U test was used for between-group comparisons. Categorical variables were compared with chi-square test and Fisher’s exact test. For the evaluation of correlations between biomarkers Spearman’s correlation coefficient was used. A ratio was calculated between the concentration of the biomarker (LA post-ablation) and the Trop I level (6 h post-ablation) to reflect the coagulation activity in relation to the size of the lesion (myocyte destruction). A P value <0.05 was considered statistically significant.

Owing to the exploratory and hypothesis generating nature of this study, power calculations and adjustments for the multiplicity of statistical analyses were not made.

Results

Patients

Fifteen patients were allocated to ablation with the cryoballoon and 15 to ablation with the RF PVAC. The baseline demographics were comparable between the two groups (Table 1), as was the pre-operative laboratory tests except for a higher B-haemoglobin level in the cryoballoon group (Table 1). One patient in each group was treated with dalteparin 200 U/kg instead of warfarin prior to ablation due to unstable INR levels.

Procedure

Complete PVI was achieved in 14 of 15 (93%) of the patients in the cryo group and 13 of 15 (87%) in the RF group. A left-sided common ostium was seen in one patient allocated to cryo and in three patients allocated to RF procedures. An additional ablation catheter using the same energy source was used in five of the cryoballoon and in five of the PVAC procedures. The procedure time and energy delivery duration was comparable for the two groups, but the ablation time was longer with the PVAC than with the cryoballoon catheter (Table 2). The INR levels on the day of the procedure were identical in the two study groups. The mean pre-procedural ACT levels and mean ACT level on the day of the procedure were identical in the two study groups. The mean pre-procedural ACT levels and mean ACT level during the procedure were comparable between the groups (Table 2). Two patients randomized to cryoablation had a DC cardioversion the day before the ablation due to ongoing persistent AF. Four patients arrived to the electrophysiology (EP) lab in AF (two in each group) and another seven patients had episodes of AF during the procedure (three in the cryoballoon and four in PVAC group). In each group, DC cardioversion was required in two patients and pharmacological conversion in two patients before the evaluation of PV conduction block. The time in AF during the procedure was 27 ± 52 and 28 ± 42 min for the cryoballoon and the PVAC group, respectively (P = 1.0). Complications related to cryoablation procedures included a major haematoma in the groin in one patient and a transient phrenic nerve paralysis, which had resolved the day after, in another patient.

Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cryoballoon (n = 15)</th>
<th>PVAC with RF (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male/female), (n)</td>
<td>11/4</td>
<td>8/7</td>
</tr>
<tr>
<td>Age, (y)</td>
<td>60 ± 8</td>
<td>62 ± 9</td>
</tr>
<tr>
<td>BMI, (kg/m²)</td>
<td>28 ± 4</td>
<td>27 ± 3</td>
</tr>
<tr>
<td>Hypertension, (n)</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>CHADS₂ score</td>
<td>0.7 ± 1.2</td>
<td>0.5 ± 0.5</td>
</tr>
<tr>
<td>Atrial fibrillation type, (n):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Persistent</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Combined</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Creatinine, (μmol/L)</td>
<td>81 ± 16</td>
<td>81 ± 18</td>
</tr>
<tr>
<td>White blood cell count, (10⁹/L)</td>
<td>5.7 ± 1.5</td>
<td>6.6 ± 1.5</td>
</tr>
<tr>
<td>Platelets, (10⁹/L)</td>
<td>267 ± 56</td>
<td>262 ± 45</td>
</tr>
<tr>
<td>Haemoglobin, (g/L)</td>
<td>147 ± 12</td>
<td>136 ± 8</td>
</tr>
</tbody>
</table>

BMI, body mass index; CHADS₂, risk score for thromboembolism; n, numbers; PVAC, pulmonary vein ablation catheter; RF, radiofrequency; y, years. Figures are mean values ± 1 SD unless otherwise stated.
No signs of thrombo-embolic events were seen during the hospital stay and no symptoms correlated to thrombo-embolic events were reported by the patients at follow-up.

Endothelial damage and platelet activation

As seen in Figure 1A, the levels and pattern of vWF antigen during the procedure were comparable in the two groups. The left atrial vWF antigen levels increased significantly after the ablation (pre- to post-ablation) in both groups. The vWF antigen levels measured in the peripheral vein after the procedure were comparable to those levels obtained at baseline in both groups. No significant differences of vWF antigen concentrations were seen between the groups at any time point ($P = 0.3–0.7$). The sP-selectin concentrations were generally slightly lower in the cryo compared with the RF group, and the difference was significant at all time points except for the v baseline, where the difference did not reach statistical significance ($P = 0.06$) (Figure 1B). In the cryo group there was a modest but significant increase in sP-selectin levels from LA pre-ablation to LA post-ablation and a similar pattern of change was observed in the RF group ($P = 0.06$) (Figure 1B). This change in sP-selectin levels from pre- to post-ablation was of comparable magnitude between the cryo group, median $9 (-2$ to $+24)\%$, and the RF group, median $8 (-6$ to $+18)\%$ ($P = 0.4$).

Markers of coagulation activity

The F1 + 2 concentration increased significantly after the transseptal puncture in both the cryo and the RF group (Figure 2A). The LA concentrations then decreased progressively throughout the procedure to reach similar levels as v baseline in both groups. The significant reduction in concentrations seen from LA baseline to LA post-ablation was comparable between the groups ($P = 0.4$). There was no difference in levels of F1 + 2 between the cryo and the RF group at any time point ($P = 0.1–0.9$). The concentrations of D-dimer were within the normal range at v baseline and remained at a similar level after the transseptal puncture both in the cryo group and in the RF group. The major changes in D-dimer levels occurred during the ablation, from LA pre- to post-ablation, when they increased by 24 (10–63)$\%$ in the cryo group and by 47 (26–54)$\%$ in the RF group. The increase was comparable between the groups ($P = 0.2$) (Figure 2B). There was no difference in the concentrations of D-dimer at the different time points between the groups ($P = 0.5–1.0$).

The coagulation activity in relation to myocardial destruction and inflammation

The Trop I level was normal in all patients pre-ablation and increased in all patients after the procedure. The levels at 6 h post-ablation were significantly higher in the cryoballoon group [median 7.95 (4.23–11.00) µg/L] than in the RF group [2.60 (1.80–3.10) µg/L] ($P < 0.001$) (Figure 3A). The CRP levels increased significantly with comparable magnitudes in both groups to similar levels at 24 h post-ablation [median 7.40 (3.40–20.00) mg/L in the cryo group].

![Figure 1](https://academic.oup.com/europace/article-abstract/15/6/798/485595/801)

**Figure 1** Concentrations of (A) vWF antigen and (B) sP-selectin at different time points during the procedure. Figures are median values with interquartile ranges. $P$ values are given for comparisons within the group between different time points.

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**Table 2** Procedure-related data

<table>
<thead>
<tr>
<th></th>
<th>Cryoballoon procedures ($n = 15$)</th>
<th>PVAC procedures ($n = 15$)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure time (min)</td>
<td>$157 \pm 32$</td>
<td>$164 \pm 39$</td>
<td>0.64</td>
</tr>
<tr>
<td>Ablation time (min)</td>
<td>$96 \pm 33$</td>
<td>$122 \pm 35$</td>
<td>0.04</td>
</tr>
<tr>
<td>Energy delivery duration (min)</td>
<td>$49 \pm 12$</td>
<td>$44 \pm 14$</td>
<td>0.34</td>
</tr>
<tr>
<td>Baseline ACT (s)</td>
<td>$127 \pm 22$</td>
<td>$125 \pm 21$</td>
<td>0.80</td>
</tr>
<tr>
<td>Mean procedure ACT (s)</td>
<td>$268 \pm 24$</td>
<td>$263 \pm 26$</td>
<td>0.59</td>
</tr>
<tr>
<td>Baseline INR level</td>
<td>$1.5 \pm 0.2$</td>
<td>$1.5 \pm 0.2$</td>
<td>0.94</td>
</tr>
</tbody>
</table>

ACT, activated clotting time; INR, international normalized ratio; n, numbers; PVAC, pulmonary vein ablation catheter.

Figures are mean values ± 1 SD unless otherwise stated.
The patient who developed a major haematoma with concomitant rise in CRP after ablation was excluded from this analysis. There was a significant correlation between the F1+2 and Trop I (r = 0.52, P = 0.01). The correlation between D-dimer and Trop I did not reach statistical significance (r = 0.41, P = 0.06).

The ratio of endothelial damage and platelet activation to cardiomyocyte destruction showed that the vWF antigen (LA post-ablation)/Trop I (6 h post-ablation) ratio was lower in the cryo group vs. in the RF group, as was the sP-selectin/Trop I ratio. The same pattern was seen for the coagulation activity to cardiomyocyte destruction ratio, where the cryo group showed a lower D-dimer/Trop I ratio than the RF group (Table 3).

Table 3 Ratios between biomarker and Trop I

<table>
<thead>
<tr>
<th></th>
<th>Cryoballoon</th>
<th>PVAC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>vWF antigen</td>
<td>0.2 (0.1–0.2)</td>
<td>0.5 (0.4–0.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>sP-selectin</td>
<td>3.3 (1.9–5.0)</td>
<td>12.3 (9.1–20.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>D-dimer</td>
<td>48.4 (38.7–56.9)</td>
<td>127.9 (79.0–236.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Calculated ratios between biomarker sample from the left atrium post-ablation and Trop I 6 h post-ablation.

PVAC, pulmonary vein ablation catheter; RF, radiofrequency; sP, soluble plasma; vWF, von Willebrand factor.
Figures are median values (interquartile range).
Discussion

In this study, we compare two ablation catheters for AF ablation using different energy sources, the cryoballoon (cryoenergy) and the PVAC (RF energy), with regard to their effects on coagulation, inflammation, and myocardial destruction.

The major findings in this study are that there seemed to be no major differences in the overall activation of the coagulation system between the two ablation groups even though the cryoballoon caused a more pronounced myocardial destruction than the PVAC. Our finding that the cryoballoon resulted in a more pronounced myocardial injury than the PVAC, as indicated by the higher Trop I level post-ablation, is supported by a recent study reporting significantly higher Trop I levels after ablation with the cryoballoon when comparing the same ablation catheters. The higher Trop I levels may reflect the larger contact surface between the cryoballoon catheter and the endocardial tissue than what is obtained with the PVAC catheter. Two other studies have analysed Troponin T levels after AF ablation with a cryoballoon vs. pairwise encircling of the ipsilateral PVs using an irrigated tip RF ablation catheter. In one of these studies the Troponin T levels were comparable between the groups, but in the other higher after RF ablation. The divergent results in our study as compared with the later may reflect the different technique and mode of RF energy used and also relate to the operator-dependent difference in number of RF applications given to achieve PVI.

The inflammatory response, measured by CRP levels, was comparable between the groups, which is consistent with other studies. The biomarkers, taken at five different time points during the ablation procedure in our study, were chosen to cover the different parts of the coagulation cascade: endothelial damage (vWF), platelet activation (sP-selectin), thrombin generation (F1+2), and global activation of coagulation and fibrinolysis (D-dimer).

In our study the measured levels of vWF and the pattern of change during the procedure were comparable between the groups. A calculated ratio between vWF and Trop I was however higher for the PVAC than for the cryoballoon, which may indicate a higher release of vWF per volume myocardial injury, or per inner surface area. Since vWF mainly reflects the disruption of the endothelium, such a finding would be consistent with a previous morphological study, which describes that the endothelial surface is kept more intact after a cryolesion than what is seen after a RF energy lesion using a non-irrigated ablation catheter.

The main activation of platelets, as reflected by sP-selectin, displayed a similar pattern between the two groups with an in general relatively constant level during the procedure. Since thrombin is a major stimulus for P-selectin expression on platelets, one would have expected a raise in sP-selectin during the procedure, but as heparin has been shown to reduce sP-selectin, it may well explain this pattern. There is no obvious explanation for why the sP-selectin levels were higher from the start and throughout the procedure in the PVAC group than in the cryo group. Previous studies have shown that AF itself causes local cardiac platelet activation within minutes of its onset as reflected by a raise in sP-selectin and F1 + 2. Yet no differences were found between the groups with regard to the AF type or pattern, or with regard to the number of patients presenting with ongoing AF on admission to the hospital or to the EP lab. Concerns have been made regarding the use of contrast media, as it may have a prothrombotic effect by the activation of platelets. In vitro studies have, however, shown that in comparison with other contrast media, loxaglate, which is used during cryoballoon procedures, does not show any increase in the expression of P-selectin on the platelet surface or platelet aggregation.

Prothrombin fragment 1 + 2, a marker of thrombin generation and a central part of the coagulation process, was increased after the transseptal puncture and then decreased during the procedure, which probably reflects the effect of heparin. D-dimer reflects the final stage of the coagulation cascade. Even though there was an increase in D-dimer during the ablation, the median levels were still beneath what is clinically considered the upper normal limit for D-dimer (<500 µg/L). Levels >500 µg/L of D-dimer have been shown to be predictive of thrombo-embolic events in patients with permanent AF during oral anticoagulation.

In our study, such levels were observed in three patients from baseline and only in another three patients, distributed in both groups, the levels increased to >500 µg/L post-ablation. Two previous AF ablation studies have compared the cryoballoon catheter with a RF ablation catheter used for the point-by-point technique, with regard to their effects on coagulation and platelet activation. Siklody et al. showed comparable response in biomarkers using an irrigated RF ablation catheter vs. the cryoballoon, whereas Tse et al. described that a non-irrigated RF ablation catheter seemed to cause more persistent platelet activation than the cryoballoon. The PVAC, having a phased RF mode, used in our study, may differ from other RF energy catheters with regard to its effect on tissue and activation of coagulation and platelets.

Apart from the direct effect of ablation, several other factors may contribute to increased levels of biomarkers during a procedure, such as puncture of vessels and atrial septum, exposure to foreign materials, time and as previously mentioned, the AF itself. Since the procedure was standardized regarding numbers and types of diagnostic catheters and sheaths, and since similar procedure times and peroperative AF durations were seen between the groups, one can anticipate that a difference in activation of the biomarkers would mainly reflect the different energy sources used for ablation.

The procedure times for PVAC ablation seen in our study were the upper range of what has previously been reported. A plausible explanation may be that our patients were awake during the procedure and despite analgetics often experienced intolerable pain during RF application, necessitating interruption of energy delivery. This problem was more common when all electrode pairs were used simultaneously, and consequently, a limited number of pairs were often used for energy delivery, resulting in a higher number of applications. Recent studies have shown a significantly higher incidence of silent cerebral emboli on magnetic resonance imaging associated with the PVAC compared with both the cryoballoon and irrigated RF ablation catheters after AF ablation procedures. The mechanisms of these emboli are not well understood even though...
different theories such as charring (carbonization of the catheter), air embolism, or an energy-dependent risk of thrombus formation on the ablation site have been discussed.\textsuperscript{1,3} Our findings do not support a higher degree of activation of coagulation with the use of the PVAC as compared with the use of the cryoballoon.

In an attempt to estimate coagulation activity, endothelial damage, and platelet activation per lesion size, we used biomarker ratios to Trop I, where Trop I was used as an indirect measure of lesion size, either surface or depth. Even though this ratio is not a standardized measure, one may speculate, from the differences seen, if the lesions produced by the PVAC were indeed more thrombogenic per se than the cryoballoon. Whether such difference is of any clinical importance is, however, doubtful since the goal to achieve complete PVI was reached by both techniques with a comparable total activation of the coagulation system.

**Limitations**

This study was limited to an evaluation of the coagulation system during the ablation procedure. In fact thrombo-embolic events do occur even weeks following an ablation.\textsuperscript{2} Even though no major differences were seen between the different energy sources used, it cannot be ruled out that such differences may appear during the healing phase. Lesions produced by cryo and RF energy develop in different ways and during different time course why further sampling after the completed procedure may have added valuable information, especially after the reports of silent emboli. These reports were, however, not available when designing this study. The size of this study was small and was considered an explorative study and as such was not powered to show minor differences between the two ablation techniques.

**Conclusion**

Even though the cryoballoon catheter causes a more extensive myocardial damage than the PVAC, there seems to be no major difference in the overall activation of the coagulation and inflammatory systems between these two ablation catheters, according to this study.

Whether the overall relatively small effects on the coagulation system, as seen in our study, may be sufficient to result in thromboembolism, and whether the higher ratios of coagulation activity per myocardial lesion size seen with the PVAC implies more thrombogenic lesions is unclear and warrants further studies in larger patient populations.

**Conflict of interest:** none declared.

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**References**