BG Pulse Journal USA
ISSN:1947-2536 http://www.bgpulseusa.com/index.php/bg
BG PULSE JOURNAL

SAFETY PROFILE OF PULSED FIELD ABLATION IN ATRIAL FIBRILLATION: PROCEDURAL COMPLICATIONS, TISSUE SELECTIVITY AND EMERGING CLINICAL CHALLENGES

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Doi: https://doi.org/10.5281/zenodo.24195577

Abstract: Pulsed field ablation (PFA) is a non-thermal catheter-based technique increasingly used for pulmonary vein isolation in patients with atrial fibrillation (AF). Its mechanism, irreversible electroporation, offers relative myocardial tissue selectivity and may reduce several complications associated with thermal ablation. Nevertheless, PFA should not be considered free of procedural risk. This review examines the safety profile of PFA with emphasis on vascular injury, cardiac tamponade, thromboembolic events, coronary artery spasm, haemolysis and acute kidney injury, as well as the reduced occurrence of oesophageal injury, pulmonary vein stenosis and persistent phrenic nerve palsy reported in large registries. The MANIFEST-17K registry, which included 17,642 patients, reported a major complication rate of approximately 1%, with tamponade, vascular events, stroke and coronary spasm among the relevant events. Rare haemolysis-associated renal failure was also identified. These findings demonstrate that PFA changes rather than eliminates the complication profile of AF ablation. Safe implementation requires appropriate patient selection, anticoagulation, vascular-access technique, intraprocedural monitoring and postprocedural surveillance. Continued registry reporting and long-term comparative studies are needed to clarify uncommon adverse events and improve procedural standards.

Keywords: Atrial fibrillation; pulsed field ablation; safety; complications; coronary spasm; haemolysis; acute kidney injury; catheter ablation.

Introduction

Catheter ablation is an established treatment option for symptomatic atrial fibrillation (AF), particularly when rhythm-control treatment is required and antiarrhythmic drugs are ineffective, poorly tolerated or not preferred. Radiofrequency and cryoballoon techniques have been widely used to achieve pulmonary vein isolation (PVI), but thermal energy can injure structures adjacent to the left atrium[1].Pulsed field ablation (PFA) uses short, high-voltage electrical pulses to induce irreversible electroporation. Because myocardial cells may be more susceptible to the applied electrical field than some surrounding tissues, PFA has the potential to reduce collateral thermal injury. This tissue-selective effect has generated particular interest regarding oesophageal damage, phrenic nerve injury and pulmonary vein stenosis.However, the safety of PFA must be evaluated across the entire procedural pathway[2,3]. Transseptal access, catheter manipulation, anticoagulation, vascular access and left atrial instrumentation continue to carry risks. In addition, PFA has been associated with energy-specific events, including coronary vasospasm and haemolysis. This review summarizes the available evidence and discusses practical implications for risk reduction.Evidence from large-scale clinical registries

The MANIFEST-17K study provides one of the largest real-world assessments of PFA safety. It included 17,642 patients treated at 106 centres using a pentaspline catheter. Major adverse events were reported in approximately 0.98% of patients. The most frequent major events included

pericardial tamponade (0.36%), vascular complications requiring intervention (0.30%), stroke (0.12%) and coronary artery spasm (0.14%). Mortality was reported in 0.03%.[4]

Notably, no oesophageal fistula or dysmotility, pulmonary vein stenosis or persistent phrenic nerve injury was reported in this cohort. Transient phrenic nerve palsy was uncommon. These findings are consistent with the proposed tissue-selective properties of PFA, although registry data cannot establish that the risk of every complication is zero or directly prove superiority over thermal technologies.he registry also identified complications that require specific awareness. Coronary spasm and haemolysis-associated acute renal failure were uncommon but clinically important. The findings reinforce the need for continued surveillance as PFA is adopted in broader populations and across different procedural settings.Cardiac tamponade and vascular complications.Cardiac tamponade remains a potential complication of any left atrial catheter ablation procedure. It may result from transseptal puncture, guidewire manipulation, catheter advancement or direct cardiac injury. In MANIFEST-17K, tamponade occurred in 0.36% of patients, and most cases were managed by pericardiocentesis[5]. This demonstrates that non-thermal energy does not remove mechanical risks associated with catheter-based intervention.

Vascular complications are also relevant because PFA requires venous access and large-bore sheath systems in many workflows. Haematoma, pseudoaneurysm, arteriovenous fistula and bleeding may occur. Ultrasound-guided vascular access, careful sheath management, appropriate haemostasis and postprocedural assessment can reduce avoidable access-related injury. In MANIFEST-17K, centres routinely using ultrasound guidance had a lower rate of major vascular complications than centres not routinely using it; this observational finding supports, but does not by itself prove, the benefit of ultrasound guidance[7].

Thromboembolic and neurological events

Stroke and transient ischaemic attack remain important complications of AF ablation. Potential mechanisms include thrombus formation on catheters or sheaths, air embolism, tissue debris and inadequate anticoagulation. PFA does not eliminate these mechanisms. In MANIFEST-17K, stroke was reported in 0.12% of patients. The low frequency of clinical stroke should not be interpreted as absence of subclinical cerebral injury, which has been detected in some imaging substudies.

Procedural safety depends on meticulous anticoagulation management, adequate intraprocedural activated clotting time according to the applicable protocol, careful flushing and de-airing of sheaths, and minimizing unnecessary catheter exchanges. Blood-pressure control and prompt neurological assessment are also important. Anticoagulation after ablation should be determined by the patient's thromboembolic risk and guideline recommendations, not solely by apparent rhythm success[6]

Coronary artery spasm

Coronary artery spasm is a recognized energy-specific concern with PFA, particularly when applications are delivered near coronary arteries. The mechanism is not completely understood, but electrical-field exposure and local vascular responses have been proposed. In MANIFEST-17K, coronary spasm was reported in 0.14% of patients. Although uncommon, it can cause myocardial ischaemia, electrocardiographic changes and haemodynamic instability.

Risk mitigation includes understanding the anatomical relationship between the intended lesion set and coronary structures, avoiding unnecessary applications in high-risk locations and maintaining appropriate haemodynamic and electrocardiographic monitoring. Suspected spasm requires prompt recognition and management according to established interventional cardiology practice. The evidence base remains insufficient to define a universal preventive medication strategy for all PFA procedures[5].

Haemolysis and acute kidney injury

Haemolysis is another complication that has been reported with PFA. Electrical pulses may cause red blood cell injury, leading to release of free haemoglobin. In severe cases, pigment-related renal injury may occur. MANIFEST-17K reported haemolysis-associated acute renal failure requiring temporary haemodialysis in a small proportion of patients (0.03%); the affected patients were reported to recover.Potential risk-reduction measures include avoiding unnecessary excessive pulse delivery, maintaining appropriate hydration when clinically suitable and considering renal function in preprocedural assessment. In patients with suspected significant haemolysis, evaluation may include haemoglobin, lactate dehydrogenase, bilirubin, haptoglobin, urinalysis and renal-function testing. These investigations should be guided by clinical findings and local protocols; routine extensive testing in every uncomplicated case has not been established by the registry evidence.One of the proposed advantages of PFA is a lower risk of thermal injury to adjacent structures. In MANIFEST-17K, no oesophageal fistula or dysmotility, pulmonary vein stenosis or persistent phrenic nerve palsy was reported. Transient phrenic nerve injury was rare. These observations are reassuring and consistent with preclinical evidence of relative tissue selectivity.Nevertheless, the absence of events in a registry does not prove that a complication is impossible. Rare events may be missed, underreported or occur with different catheter designs, waveforms and lesion strategies. Operators should continue to follow established procedural precautions, monitor diaphragmatic function when relevant and investigate symptoms suggestive of oesophageal or pulmonary complications[6].

Practical framework for procedural safety

Safe PFA requires a structured approach before, during and after the procedure. Before ablation, clinicians should assess AF type, comorbidities, renal function, anticoagulation, vascular anatomy and the patient's overall procedural risk. Informed consent should explain both established catheter-ablation risks and complications that may be more specific to PFA.

During the procedure, essential safety measures include image-guided or ultrasound-guided vascular access where appropriate, careful transseptal puncture, continuous haemodynamic monitoring, appropriate anticoagulation, meticulous sheath flushing and confirmation of catheter position. Operators should be familiar with the specific catheter system and its recommended energy-delivery parameters.After the procedure, monitoring should address vascular access-site bleeding, pericardial effusion or tamponade, neurological symptoms, rhythm disturbances and renal complications when clinically indicated. Clear discharge instructions and timely follow-up are important. Institutional complication registries and multidisciplinary review can support continuous quality improvement[3].

Limitations of current evidence

Randomized trials are generally designed to compare efficacy and common safety outcomes, but they may be underpowered to detect rare complications. Large registries provide broader real-world experience but may be limited by retrospective data collection, variable definitions and incomplete event ascertainment. Comparisons across studies are further complicated by differences in catheter platforms, energy waveforms, operator experience, patient selection and lesion sets.Accordingly, the safety profile of one PFA system should not automatically be assumed to apply identically to all PFA technologies[4]. Future research should use standardized definitions, independent event adjudication, systematic neurological and renal assessment where appropriate, and longer follow-up. Comparative studies should also distinguish energy-specific complications from risks inherent to transseptal catheter procedures.

Conclusion

PFA has a favorable and distinctive safety profile, with large registry data showing very low rates of several complications traditionally associated with thermal injury, including oesophageal injury, pulmonary vein stenosis and persistent phrenic nerve palsy. Nevertheless, tamponade, vascular injury and thromboembolic events remain relevant, while coronary spasm and haemolysis-associated renal injury require specific awareness. PFA should therefore be regarded as a technology with a different, rather than risk-free, complication profile. Careful procedural technique, anticoagulation, monitoring and postprocedural surveillance remain essential. Continued randomized research and large-scale registries are necessary to define uncommon risks and optimize patient safety.

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