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EDITORIAL

Deep sedation for pulsed field ablation by electrophysiology staff: can and should we do it?

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Pulsed field ablation (PFA) is a new, non-thermal ablation modality for pulmonary vein isolation (PVI) in patients with atrial fibrillation (AF).[1–4] A recent registry demonstrates an encouraging single-procedure success rate with a good safety profile and short procedure times in a real-world AF patient population.[3] Also, it appears that there are less energy-related side-effects with PFA.[2,3,5] Procedures in this European registry were performed either under general anaesthesia or deep sedation using a continuous propofol infusion.[3] This may limit the use of this technique in centres where general anaesthesia or deep sedation with propofol is not available or may not be administered by an electrophysiology staff. Therefore, other sedation techniques with e.g. midazolam or dexmedetomidine may be used to facilitate the increasing use of PFA for AF. A recent EHRA survey showed that 66% of patients undergo PVI with conscious/deep sedation (unknown which sedation techniques were used), 24% with general anaesthesia, and 10% with local anaesthesia only. Implying, that more than 90% of patients (and/or operators) choose a form of sedation for PVI.[6] Another worldwide survey showed that concerning the legal requirements for deep sedation, 59.6% stated that the presence of an anaesthesiologist was necessary, 16.8% centres stated that a specially trained nurse could perform deep sedation without the presence of anaesthesiologist, 11.8% responded that the presence of a second physician in the electrophysiology allowed them to perform deep sedation without an anaesthesiologist, and only 11.8% answered that the electrophysiologist could perform deep sedation by himself without additional personnel.[7] Besides legal requirements, the sedative effects of propofol and midazolam/dexmedetomidine are different. Propofol is shown to have a relatively low cumulative need for positive pressure ventilation and intubation.[8] Midazolam, on the other hand, is known for inadequate sedation.[8] Dexmedetomidine can also be used and has been shown to provide (in combination with remifentanil) deeper sedation, less respiratory depression, better analgesia, and higher procedural satisfaction for electrophysiologists during PVI as compared to midazolam (in combination with remifentanil).[9] All these studies have been performed before PFA was introduced; as PFA needs deeper sedation than during cryoballoon or radiofrequency ablation data on other sedation strategies are needed.[2,3] However, with some PFA techniques, muscle spasms appear to be more limited; implying that deepness of sedation might be tailored according to the PFA system used.

In this issue of *Europace*, two research letters from two different Italian groups are presented by Grimaldi *et al.*[10] and Iacopino *et al.*[11] using sedation strategies based on midazolam or dexmedetomidine. Grimaldi *et al.*[10] showed that using a strategy based on midazolam (in combination with other drugs) before entering the electrophysiology lab and dexmedetomidine and remifentanil inside the electrophysiology lab was safe to use with excellent patient satisfaction (*Table 1*). There is a disclaimer given and that is that all staff was trained in management of cardiac sedation and advanced life support and an anaesthetic consultant was available onsite. In the paper by Iacopino *et al.*, the sedation technique was also based on midazolam, however, an anaesthesiologist was available in the room. The sedation was structured in three main steps as follows: preparation to femoral puncture, femoral puncture to trans-septal puncture, and ablation of the pulmonary veins (*Table 1*).[11] Different to the paper by Grimaldi *et al.* was that Iacopino used ketamine (5 min) before the first PFA applications (3rd step). In total, patients were sedated less than an hour, as it was safe and effective sedation and both patient and operator were satisfied. Primary reason for both papers not to use propofol is the risk for respiratory depression and it is also for that reason that many European countries only allow anaesthesiologist to use propofol (and the same holds for ketamine, dexmetomidine, and remifentanil) to ensure patient safety during procedures. However, there is no uniformity on this aspect in Europe.

The authors from both papers should be congratulated for their important contribution to the field. There are, however, based on both papers, some important limitations to consider before implementing a midazolam- or dexmedetomidine-based sedation. In the paper by Grimaldi *et al.*, mean BMI was 26. As a BMI above 30 is shown to be associated with requirement of non-invasive ventilation or endotracheal intubation, this is something to take into consideration when planning a sedation strategy.[12] Whether or not it is safe to perform this midazolam strategy by non-anaesthesiologists in these patients with a higher BMI, e.g. >30, is therefore unknown. Mean BMI was higher (29) in the paper by Iacopino, however, in this study, an anaesthesiologist was present in the room. During PFA procedures, sedation should

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Table 1 Comparison of both strategies

	Grimaldi *et al.* ($n = 29$)	Iacopino *et al.* ($n = 65$)
Pre-electrophysiology lab/pre-femoral puncture	Midazolam 2 mg Ondansetron 4 mg Dexamethasone 4 mg	Midazolam 2 mg Fentanyl 1 μg/kg
Femoral puncture to trans-septal puncture	Remifentanil 0.5 ng/mL dexmedetomidine 1 μg/kg/h	Fentanyl 0.5–1.0 μg/kg
PVI		Midazolam 1–2 mg Ketamine 1.5–2 mg/kg Atropine 1 mg
Anaesthesiologists	On site	In the room
Adverse reaction	None	One patient switched to propofol
PFA system	Multi-Channel PFA Generator (PFA Generator; Biosense Webster, Inc.; Irvine, CA)	FARAPULSE (Boston Scientific, MN, USA
Pulse type	Short-duration, high-voltage *bipolar* biphasic pulses	Biphasic waveform on a microsecond scale

PFA, pulsed field ablation; PVI, pulmonary vein isolation.

be as deep as possible keeping the balance between deep enough sedation vs. prolonged periods of apnoeas might be particularly challenging for non-anaesthesiologists and might also not be in the comfort zone of a team without anaesthesiologists. Also, the patients in both papers appear to be younger (Grimaldi mean age was 55 and Iacopino 59), as compared to recent all-comers in the EU-PORIA registry (mean age 66).[3] While this may not be a severe limitation, it appears that most patients in both papers were not only of younger age but also had less co-morbidities. Offering a midazolam/dexmedetomidine-based deep sedation strategy might therefore be particular interesting in those patients. Whether or not older patients have more co-morbidities (e.g. heart failure with reduced ejection fraction), this strategy might also be applicable has to be seen. Furthermore, both studies have a relatively small sample (29 and 65 patients) size with no (historical) control group and did not make use of randomization. This would be a field of future research as randomized trials comparing midazolam vs. propofol for PVI are sparse. Only in 2007, a prospective randomized trial randomized 120 patients to two sedation strategies, propofol infused deep sedation vs. midazolam in combination with fentanyl for conscious sedation. Two patients in the propofol group required positive pressure ventilation for desaturation compared to one patient in a midazolam group.[13] Another interesting aspect will be a tailored sedation approach for PFA procedures. As procedure times are shorter than cryoballoon or radiofrequency, there might be an opportunity for a very short, very deep sedation protocol for PFA procedures. This might also depend on the type of PFA that is being used. Another aspect that is worth noting is that in both studies, only PVI was performed. With PFA, we now observe a shift in additional lesions (posterior wall isolation, mitral line, and roof line) that may need different or deeper sedation than during a PVI only approach.[2,3,14]

What should be the next step before implementing this in clinical practice? Moving the needle forward in this field needs an adequately powered randomized trial comparing propofol vs. midazolam- or dexmedetomidine-based deep sedation strategy in patients undergoing PVI with PFA. Endpoints for this trial should not only include safety of the procedure (hypoxia or need for positive pressure ventilation/intubation) but also patient and electrophysiological staff satisfaction. Also, the additional value of an anaesthesiologist in or outside the room in more difficult cases should be investigated in more detail before this should be implanted to a larger scale.

In conclusion, both groups show that when electrophysiology staff is adequately trained, we can safely perform deep sedation with midazolam or dexmedetomidine. Whether we should do it without an anaesthesiologist (in the room) or a fully dedicated team on sedation techniques should be further investigated.

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