



Energy titration strategies with the endoscopic ablation system: lessons from the high-dose vs. low-dose laser ablation study

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Aims

To assess the effects of low-dose (LD) and high-dose (HD) ablation on acute and chronic success in patients with atrial fibrillation (AF). While the concept of visually guided pulmonary vein isolation (PVI) has been established little is known on energy titration using laser ablation.

Methods and results

In 60 patients with AF, PVI using the endoscopic ablation system (EAS) was performed in two groups. Visually guided ablation was carried out after obtaining optimal tissue contact with 5.5–8.5 W in the LD group and with >8.5 W in the HD group. Acute PVI after a single visually guided circular lesion set was achieved in 89% (HD) and 69% (LD), respectively, ($P = 0.0004$). In 70 and 39% of patients all PVs were isolated after a single ablation circle in the HD and LD group, respectively, ($P = 0.009$). After gap ablation all PVs were isolated with the EAS. More energy was deployed (6483 ± 1834 vs. 5306 ± 2258 Ws; $P \leq 0.0001$) with less applications (31.6 ± 8 vs. 35.2 ± 15 applications per PV; $P = 0.03$) leading to shorter procedure times (128 ± 17 vs. 154 ± 38 min; $P = 0.001$).

During median follow-up of 311 days (261–346) recurrence rate was 17 and 40% in the HD and LD group, respectively. In both groups one phrenic nerve palsy was observed.

Conclusion

For the first time, it was demonstrated that high ablation power affects acute and chronic outcomes. High-dose laser balloon ablation allows for an acute PVI rate of 89% solely by visually guided circular ablation and is associated with a chronic success rate of 83% after a single procedure.

Keywords

Ablation • Atrial fibrillation • Laser • Balloon catheters • Energy titration

Introduction

In various reports the concept of visually guided ablation using the endoscopic ablation system (EAS; HeartLightTM, CardioFocus, Marlborough, MA, USA) for pulmonary vein isolation (PVI) was introduced and different ablation strategies including circumferential and sequential PVI were described.^{1–3} Most recently, the degree of PV occlusion (contact) and the number of catheter repositionings (stability) were identified as predictors of acute ablation success.⁴ In this feasibility study, suboptimal contact could not be compensated by higher ablation power or more energy applica-

tions. Moreover, little is known on the influence of varying ablation power on the acute and chronic success in atrial fibrillation (AF) ablation.

Therefore, we sought to determine the role of different energy dosing regimens during visually guided balloon ablation with optimal contact on the acute and chronic outcome in patients with drug refractory AF.

Patients and methods

The study was approved by the local Institutional Review Board. All patients gave written informed consent prior to the procedure.

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What's new?

- High dose laser ablation leads to an 89% acute PVI rate only using visually guided ablation without additional mapping.
- The long-term clinical success rate of HD ablation is superior to LD ablation, showing an 83% AF free survival after a single procedure.

Inclusion and exclusion criteria

Patients with symptomatic drug refractory paroxysmal AF and aged 18–70 years without previous PVI attempt were enrolled. In addition, the study protocol allowed inclusion of patients with electrically or chemically cardioverted AF within 7 days after its onset (per definition persistent AF). At least one AF episode had to be documented within the past 6 months. Left atrium (LA) size had to be <50 mm. Patients with evidence of structural heart disease (except for stable coronary artery disease) and a reduced left ventricular function <30% or valvular dysfunction >II° were excluded.

Pre-procedural imaging

All patients underwent transthoracic and transoesophageal echocardiography to rule out LA thrombus the day before the procedure.

Electrophysiological procedure

The ablation procedures were performed under sedation using boluses of midazolam and fentanyl as well as continuous infusion of propofol 1%. An oesophageal temperature probe (SensiTherm™, St Jude Medical, Minnetonka, MA, USA) was inserted. If oesophageal temperature exceeded 39°C energy delivery was terminated. To complete the circular ablation energy was reduced and/or the balloon size varied to prevent further oesophageal heating.

After placing 6 F decapolar catheters into the coronary sinus and along the His bundle region, a single transseptal puncture was performed. An 8 F sheath (SL1; St Jude Medical) was introduced into the LA. Heparin was administered to maintain activated clotting time between 300 and 350 s. Selective PV angiography was performed to identify the PV ostia. A spiral mapping catheter (Biosense Webster, Inc. Diamond Bar, CA, USA) was placed at the PV ostium to record PV potentials using a computerized EP-system (Axiom Sensis XP, Siemens, Erlangen, Germany).

The transseptal sheath was then exchanged via a guidewire placed in the left superior PV, (LSPV) for a 12 F (15 F outer diameter) steerable sheath. The second 8 F sheath in the femoral vein was exchanged to the long 8 F transseptal sheath and placed in the superior vena cava carrying a diagnostic catheter to perform phrenic nerve (PN) stimulation (20 mA, 2.9 ms) during ablation of the right superior PV (RSPV). If loss or weakening of capture was observed, energy delivery was instantaneously terminated.

The endoscopic ablation system

The details of the EAS have been described in detail elsewhere.³ Briefly, it consists of a non-steerable, compliant balloon catheter

with a range of diameters from 9 to 35 mm. After introduction into the LA via a steerable 12 F sheath it is filled and continuously flushed with deuterium (D₂O) for cooling purposes. The central catheter shaft houses a 2 F fibre optic endoscope which enables direct visualization of the PV antrum once the balloon has been inflated. Laser energy can also be delivered via a second fibre from a 980 nm, laser diode source.

Ablation and dosing

The EAS was positioned at each individual PV ostium to perform ablation. Optimal PV occlusion (category 1 or 2) with maximal exposure of LA tissue was attempted. As recently suggested, the degree of PV occlusion/LA tissue exposure was categorized according to the visual impression as follows: (i): 360°; (ii): 270–359°; (iii): 180–269°; (iv): <180°. Under visual guidance ablation lesions were deployed in a contiguous manner by overlapping the individual lesions by 30–50%. Overlapping was facilitated using the LightTrack™ (CardioFocus) software enabling visualization of energy delivery location and review by fusion of screenshots of any individual ablation site.

Patients were prospectively assigned to two groups in a 1:1 fashion: after obtaining optimal tissue contact, ablation energy was titrated from >8.5 to 12 W in the high-dose (HD) group and in the low-dose (LD) group energy was titrated from 5.5 to ≤8.5 W. Ablation energy was reduced in case of too narrow exposure of periostial myocardium despite optimal occlusion in order to avoid thermocoagulation or balloon damage (Figure 1). In addition, if laser applications behind the catheter shaft could not be avoided lower energy levels (5.5–8.5 W) were chosen in the HD group.

The number of applications and the total energy deployed was collected for each individual PV. In all patients PVs were treated in the following sequence: LSPV, left inferior PV, RSPV and right inferior PV. If a left common PV was present, it was treated first.

Post-procedural care

After echocardiographic exclusion of pericardial effusion, oral anticoagulation with phenprocoumon was resumed targeting an

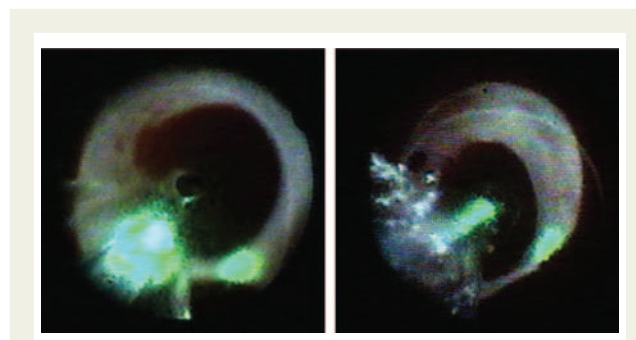


Figure 1 Endoscopic view to the left superior pulmonary vein with optimal occlusion. Left panel: Broad corridor of atrial myocardium exposed allowing for high-dose ablation along the whole circumference. Right panel: Despite optimal occlusion (360° view) partially narrow zone of myocardium (4–6 o'clock) requiring dose reduction to avoid balloon heating or thermocoagulation.

international normalized ratio (INR) of 2–3 for at least 3 months. Alternatively, novel oral anticoagulants (dabigatran or rivaroxaban) were prescribed at the discretion of the physician. Low-molecular-weight heparin was administered in a therapeutic dose until a therapeutic INR of 2–3 was reached. Antiarrhythmic drug therapy was discontinued immediately after the procedure.

Study endpoints

The acute primary endpoint was the number of isolated PVs after a single, purely visually guided ablation circle around the individual PV. The chronic primary endpoint was freedom from AF lasting longer than 30 s off antiarrhythmic drug after a blanking period of 90 days post-ablation.

Secondary endpoint included procedural characteristics as well as safety data including peri-procedural complications.

Follow-up

At day 90, patients attended an outpatient visit including a 72 h Holter electrocardiogram (ECG). At 3, 6, and 12 months patients were scheduled for outpatient visits including a 72 h Holter ECG. In case of symptoms patients were equipped with a transtelephonic event recorder (loop 3300 BT, Vitaphone, Mannheim, Germany) to submit ECGs during symptomatic episodes. The physicians performing the follow-up were blinded to the individual dosing regimen.

Statistical analysis

Data mean \pm standard deviation was used to describe continuous variables with normal distribution; otherwise median and inter-quartile ranges were used. For diagnostic parameters the absolute and relative frequency were counted. For between-group comparisons parametric and non-parametric tests were used as appropriate (for details, see Results). Multiple group comparisons were performed using one-way analysis of variance and Tukey's multiple comparison test.

Results

In total, 60 patients were enrolled and assigned to two groups. The patient characteristics are displayed in Table 1. It is of note, that more patients with persistent AF (26 vs. 7%) and more male patients (70 vs. 40%) were treated in the HD group.

Acute outcome

After a single visually guided circular ablation around the individual PV 103 of 116 (89%; HD) and 82 of 118 (69%; LD) PVs were acutely isolated (Figure 2; $P = 0.0004$). The chance of achieving PVI with HD was 3.5 higher than with LD (Fisher's exact test, odds ratio = 3.5; confidence interval 1.7–7.0). After gap mapping and ablation all 234 PVs were acutely isolated using EAS.

Using HD, the total number of energy applications ($P = 0.004$) was lower (31.6 ± 8 vs. 35.2 ± 15 applications per PV; $P = 0.03$) but the total ablation energy applied per PV was significantly higher (6483 ± 1834 vs. 5306 ± 2258 Ws; $P \leq 0.0001$, Figure 3). In summary, the mean power per application was 10.7 ± 1 and 7.6 ± 1 W in the HD and LD group, respectively, ($P = 0.003$).

Table 1 Patient characteristics

	Low dose (n = 30)	High dose (n = 30)	P
Male gender	12 (40%)	21 (70%)	0.02
Age	62 \pm 8	64 \pm 9	0.32
Persistent AF	2 (7%)	8 (26%)	0.08
Median AF duration	3 (1–6)	2 (–5)	0.06
LV-EF (%)	67 \pm 8	62 \pm 7	0.06
LA-size (mm)	39 \pm 5	41 \pm 4	0.07

AF, atrial fibrillation; LV-EF, left ventricular ejection fraction; LA, left atrium.

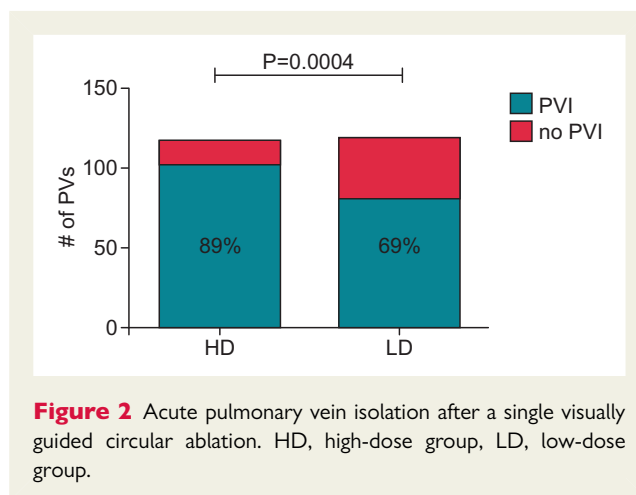


Figure 2 Acute pulmonary vein isolation after a single visually guided circular ablation. HD, high-dose group, LD, low-dose group.

After a single visually guided circular ablation all PVs per patient were isolated in 39 and 70% in the LD and HD group, respectively, ($P = 0.009$).

Procedure times were significantly shorter in the HD group (128 ± 17 vs. 154 ± 38 min; $P = 0.001$). Fluoroscopy times were 14 ± 6 min (HD) and 16 ± 6 min (LD; $P = 0.3$), respectively.

The median degree of occlusion was not significantly different between the groups (1 vs. 1; $P = 0.14$).

Procedural complications

In each group, one PN palsy occurred during ablation at the RSPV despite PN pacing. In both patients PN function had recovered after 3 months.

In the HD group, two steam pops were observed without any sequelae. Oesophageal temperature rises $>39^\circ\text{C}$ were observed in 17 (57%) and 15 (50%) patients in the HD and LD group, respectively. Most importantly, no stroke/transient ischaemic attack, tamponade or atrial-to-oesophageal fistula occurred during this study.

In the HD group, one balloon perforation occurred following a laser application too close to surrounding blood leading to local overheating at the site of energy delivery.

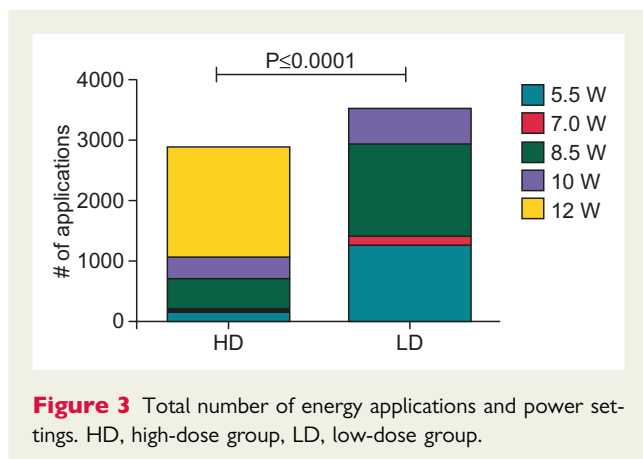


Figure 3 Total number of energy applications and power settings. HD, high-dose group, LD, low-dose group.

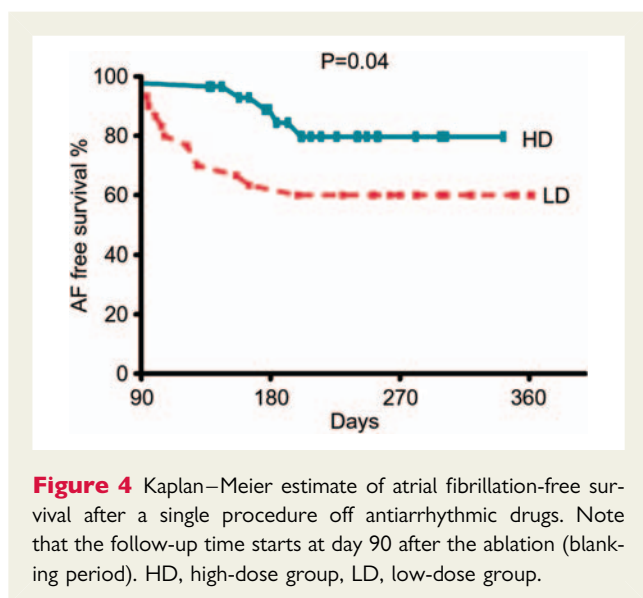


Figure 4 Kaplan–Meier estimate of atrial fibrillation-free survival after a single procedure off antiarrhythmic drugs. Note that the follow-up time starts at day 90 after the ablation (blanking period). HD, high-dose group, LD, low-dose group.

Chronic outcome

During a median follow-up of 311 days (q1–q3: 261–346 days) 5 patients in the HD group and 12 patients in the LD group experienced an AF recurrence after a single procedure off antiarrhythmic drugs. The Kaplan–Meier estimate of AF-free survival showed a statistically significant difference in favour of the HD group using the Log-rank test ($P = 0.04$; Figure 4).

No procedure-related adverse events occurred during follow-up.

In two HD and seven LD patients repeat ablation procedures were performed for AF recurrences 181 ± 86 days after the index procedure. While in the LD patients 15 of 28 PVs (54%) displayed resumed LA to PV conduction, only 1 of 7 PVs (14%) in the HD group was not electrically isolated ($P = 0.09$).

Discussion

Visually guided laser balloon ablation has demonstrated proof of concept in multiple feasibility studies.^{1–4} Little was known on

the optimal ablation energy to achieve chronically transmural lesions. The present study adds systematic data to broaden our knowledge on different dosing strategies using EAS for PVI in patients with drug refractory AF.

The major findings of the study were that (i) HD ablation is associated with a 3.5-fold higher acute success rate leading to a 89% PVI rate after a single circular ablation set around the individual PV ostium; (ii) HD ablation significantly reduced procedure times by reducing the number of required ablation lesions and the lower need for gap mapping; (iii) increased chronic success rate to 83% after a single procedure off antiarrhythmic drugs during a median follow-up of 281 days.

For radiofrequency current (RFC) ablation the role of ablation power for lesion formation was well established in experimental models.^{5,6} In contrast, *in vivo* data as well as systematic data on ablation power during diode laser ablation is scarce. Pre-clinical studies were performed *in vivo* using different energy levels ranging from 5.5 to 16 W. While lesion transmural was observed in a very high percentage of histological sections, dose-response curves were not calculated.^{1,7} The present study provides evidence that in the presence of an adequate balloon to tissue contact HD laser ablation significantly improves acute and chronic efficacy.

Most importantly, HD ablation resulted in a higher chronic success rate. Data of repeat procedures in patients with AF recurrences suggested that a higher rate of chronically isolated PVs (46 vs. 86%) in the HD group accounted for this difference. In comparison, systematic PV mapping data on all-comers demonstrated 86% durable isolation rate in a multi-centre trial.⁸

The LD follow-up data compares well to recently published data on the initial EAS experience.⁹ Notably, the horizontal course of the Kaplan–Meier curve after ~200 days is a result of a limited follow-up time rather than a definite cure from AF. However, survival curves from long-time follow-up data after RFC-guided procedures take a rather horizontal course after the first year post-ablation.¹⁰

The present study provides strong evidence on the superior acute and chronic efficacy of the HD protocol. However, due to limited animal data for an explicit HD ablation protocol and the small number of patients the general safety of HD ablation is unproven. Despite the fact that in both groups oesophageal temperature rises and PN palsies occurred at a similar rate, it remains to be determined whether HD ablation is associated with a higher incidence of oesophageal thermal injury with recent findings suggesting an incidence of 18% associated with EAS ablation.¹¹

Further, it is of note that despite optimal PV occlusion HD ablation may lead to steam pops and balloon damage most likely due to local overheating. In contrast, even in previous studies balloon failures were reported without using a particular HD protocol.^{2,3}

Pulmonary vein isolation is a widely accepted endpoint for an AF ablation procedure.¹² Using HD laser ablation 89% of all PVs were acutely isolated solely by a visually guided ablation circle. Furthermore, in 70% of patients all PVs had been isolated after purely visually guided ablation. In comparison, RFC-guided circumferential PVI ablations failed to achieve acute PVI by a single lesion set in 58% of patients if electrogram information from the disconnected circumferential mapping catheter was unavailable.¹³ This underlines the feature of the EAS to precisely deliver ablation lesions with an

optimal contact in a contiguous manner as opposed to a conventional RFC ablation catheter where variation of catheter stability and contact force might be suboptimal during various ablation lesions.¹⁴ The ability to achieve PVI in such a high number of PVs may obviate the need for a circumferential mapping catheter in the future particularly if lesion visualization is improved or the catheter tip was equipped with ring electrodes to enable PV mapping.

Conclusion

In conclusion, the present study provides strong evidence, that HD visually guided laser ablation is superior to LD ablation resulting in an acute PVI rate of 89% after a single visually guided ablation circle and a chronic success rate of 83% off antiarrhythmic drugs after a single procedure.

Conflict of interest: B.S. and K.R.J.C. received speaker's bureau from CardioFocus. Other authors declare no conflict of interest.

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