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Venous thrombosis following femoral venous access for electrophysiology studies: An on-going challenge

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In this issue of *Cardiology Journal*, Alizadeh et al. [1] report their findings prospectively comparing the risk of thrombosis following one *vs* multiple venous puncture sites for the placement of sheaths used to perform electrophysiology (EP) studies. The authors also assessed the effects of heparin on the incidence of thrombosis. *In situ* thrombosis was defined as the presence of: "a strand of thrombus connected to the tip of the catheter at the time of removal." Duplex ultrasonography was obtained 24 h after the EP study to screen for the formation of deep venous thrombosis (DVT).

The first notable finding was that subjects with multiple sheaths placed via a single venous puncture site were at greater risk of *in situ* thrombosis than those with multiple puncture sites (38% *vs* 18%). Importantly, a statistically significant reduction in the incidence of *in situ* thrombosis was observed in the single venous puncture group treated with heparin (16% *vs* 38%; $p = 0.023$), something that was not observed in the other group. The second notable finding was that no DVTs were identified in this study.

Percutaneous catheterization using the Seldinger technique was originally described by Sven Ivar Seldinger [2]. Adaptations of the guidewire method led to the development of venous catheterization that revolutionized the delivery of cardiovascular medicine. Moncrief provided one of the earliest reports of the consequences of femoral venous catheterization [3]. This report included 135 instances of femoral venous access in 91 patients. In this study, DVT was the most frequent complication, occurring in 13.3% of cases. The duration of catheter placement correlated directly with adverse events. The long-term sequelae of DVTs and deaths due to thrombophlebitis led Moncrief to conclude: "Femoral catheters should be utilized only when all other methods of intravenous infusion have been exhausted, and when in use should remain in a single femoral location for not more than seven to ten days."

Despite recent advances, vascular complications, such as hematomas, atrio-ventricular fistulae and DVTs are not uncommon following femoral venous catheterization for electrophysiology studies. Virchow's triad is a common eponym used to describe three components essential to intravascular thrombosis: inflammation of the vessel wall, stasis of blood flow, and a hypercoaguable state. Thus, placement of venous sheaths promotes vascular thrombosis by contributing to venous stasis and inciting vascular inflammation.

Studies in critically ill and trauma patients report an incidence of 9.6–26% for ileofemoral DVT formation (detected by ultrasonography) following femoral vein cannulation for central venous access, but do not comment on the incidence of thromboembolic complications [4–7]. Neither Joynt et al. [4] nor Mian et al. [6] found an association between age, gender, number of insertion attempts, length of catheter duration, or use of DVT prophylaxis and the risk of DVT formation.

Unlike critically ill populations, patients undergoing EP studies tend to be healthier and are exposed to shorter durations of indwelling catheters. Despite these differences, the incidence of asymp-

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tomatic DVT formation remains high, ranging 16––44% for ileofemoral DVT formation by ultrasonography following sheath placement for EP studies [8––10]. However, the incidence of symptomatic DVTs is much lower (0.5–0.8%). The risk of thromboembolic complications following EP procedures also remains low, ranging 0.8–1.3% [11–14]. Importantly, not all thromboembolic complications result from DVT formation. Ablation itself and left-sided procedures are independently associated with thromboembolic complications. Results from the Multicenter European Radiofrequency Survey (MERFS) provided the largest cohort of 4,398 patients referred for catheter ablation of supraventricular or ventricular tachycardias [14]. DVTs were identified in 0.5% of patients, while thromboembolic complications occurred in 0.8% of patients. The risk of embolic events following right-sided procedures was extraordinarily uncommon (0.06%) in MERFS. Importantly, this study did not provide information regarding periprocedural use of anticoagulation.

As noted above, several studies have reported a relatively frequent incidence of asymptomatic DVTs following EP studies. Chen et al. [8] reported an incidence of 17.6% for the development of asymptomatic, non-occlusive DVTs identified by duplex ultrasonography one day following invasive EP studies using multiple venous sheaths. Repeat ultrasonography at one week documented regression of the non-occlusive DVTs in 92% of cases. Embolic complications were extremely rare in this study, occurring in 0.14% of patients following radiofrequency ablation. Heparin, 5,000 U bolus followed by 1,000 U/h, was administered in all patients who underwent left-sided procedures.

A similar incidence of asymptomatic thrombosis (20%; n = 24) by ultrasonography was reported by Tiroke et al. [9] despite the use of intravenous heparin, which was titrated to a target ACT > 200 s. The risk of thrombosis was independent of age, gender, duration of study or number of sheaths. Importantly, six hours of banding were used to maintain hemostasis following sheath removal. The role of different methods used to obtain hemostasis following sheath removal (i.e. banding *vs* 15––20 min of firm pressure) has not yet been adequately studied.

The importance of intravenous heparin to minimize thromboembolic complications during left--sided procedures, specifically catheter ablation of atrial fibrillation, is well-established [15, 16]. However, its utility during right-sided EP studies remains unclear. Green et al. [11] reported an incidence of 0.8% for DVT formation in subjects who underwent radiofrequency ablation for supraventricular arrhythmias despite heparin initiated with a 5,000 U bolus followed by 1,000 U/h infusion throughout the procedure. The article by Alizadeh et al. [1] found a reduction in *in situ* thrombosis when using a single *vs* multiple venous puncture sites, but no significant differences when multiple puncture sites were used.

Low molecular weight heparin has also been shown to reduce the risk of catheter-related thrombosis. A study by Davutoglu et al. [10] reported a significantly lower incidence of venous thrombosis (18.2%; n = 2 *vs* 62.5%; n = 10; p = 0.02), assessed by ultrasound, in subjects who received a single 5,000 U injection of Dalteparin one hour prior to multiple venous sheath placement for EP study. All subjects, except one, demonstrated complete resolution following one month of anticoagulation with warfarin.

The study by Alizadeh et al. [1] adds to our understanding of the risk of thrombotic complications during EP study. First, this study suggests that the approach to femoral cannulation matters, with a reduced incidence of *in situ* thrombosis associated with multiple venous punctures compared to single puncture site. Female gender and procedure time increased the risk of *in situ* thrombosis, which should be taken into consideration. Meticulous sheath management with frequent flushing, or perhaps continuous irrigation, should be considered in such cases. It is surprising that no DVTs were identified in this study. This may reflect a limitation of the sample size, or perhaps other factors such as sheath management or methods used to achieve hemostasis following sheath pull.

In addition to the limitations of the study outlined by the authors, the presence of *in situ* thrombosis, as defined in this study, is of unclear and likely minor clinical significance. Importantly, it was not associated with DVT formation, since no subjects in the study developed DVTs.

Conflict of interest: none declared

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