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Original Article

Trans-radial versus trans-femoral access in patients with end-stage liver disease undergoing cardiac catheterization

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Abstract: Cardiac catheterization has been increasingly utilized to evaluate coronary artery disease in patients with end stage liver disease (ESLD). It is known in other populations that radial access reduces access site complications; however, there is a paucity of data in ESLD patients. We investigated vascular and bleeding complications rates between trans-femoral and trans-radial cardiac catheterizations in this high risk population. In this retrospective cohort study, three hundred and thirty four ESLD patients were identified between August 2004 and December 2012 who had undergone trans-femoral (femoral group) or trans-radial (radial group) cardiac catheterizations at our institution. The radial group was not significantly different from the femoral group in age ($p = 0.056$), proportions of genders ($p = 0.85$), and weight ($p = 0.19$); however, compared to the femoral group, the radial group had significantly lower blood pressure ($p < 0.0001$), hemoglobin (10.4 ± 1.9 vs 11.1 ± 2.02 g/dL, $p = 0.001$), and hematocrit ($30.3 \pm 5.7\%$ vs $32.6 \pm 6.0\%$, $p < 0.0006$), and had a significantly higher INR (1.94 ± 1.16 vs 1.59 ± 0.62, $p = 0.0001$). In terms of vascular complications, the radial group had a significantly lower rate of pseudoaneurysms (0% vs 3.7%, $p = 0.019$) than the femoral group. While there were no bleeding complications in either group or differences in transfusion requirements, there was a significantly lower percentage drop in hematocrit in the radial group compared to the femoral group (5.4% vs 7.8%, $p = 0.039$). In conclusion, trans-radial catheterization is associated with lower rates of vascular access site complications compared to trans-femoral catheterization.

Keywords: Cardiac catheterization, access site, end-stage liver disease

Introduction

Currently, the treatment of choice for patients with end-stage liver disease (ESLD) is orthotopic liver transplantation (OLT). As part of the workup for potential liver transplant recipients, cardiovascular assessment plays a crucial role in determining whether the patient can be expected to survive the operation and whether allocation of a scarce donor organ is appropriate [1]. Furthermore, with the increasing age and number of comorbidities (eg. cardiovascular disease) of OLT candidates, cardiac evaluation has become increasingly important [2, 3].

Associated with the high morbidity and mortality risks of OLT are hemodynamic stressors such as high resting cardiac output, low systemic vascular resistance, and sudden increased preload post-operation, underscoring the need for thorough cardiac screening [4, 5]. Initially, it was thought that liver disease was protective against coronary artery disease (CAD) due to more favorable serum lipid profiles and lower blood pressures [6-8]. However, recent studies have shown that the prevalence of CAD in ESLD patients is as high as or higher than in the general population [3, 9-11]. We reported previously that the extent of CAD (eg. multi-vessel versus single-vessel CAD) is associated with significantly higher mortality after OLT, substantiating the importance of careful pre-transplant cardiac workup [12].

Standard cardiac evaluation includes history, physical examination, electrocardiogram, chest X-ray and echocardiogram. Further workup to evaluate CAD depends on the transplant cen-

ter, but may include dobutamine stress echocardiography, nuclear myocardial perfusion imaging, computed tomography angiography, or left heart catheterization and coronary angiography. At UCSF, patients with major risk factors for CAD or abnormal noninvasive testing undergo coronary angiography for further risk stratification. Previously, we have shown that cardiac catheterizations can be performed relatively safely on ESLD patients, despite their propensity toward bleeding complications due to thrombocytopenia, reduced synthesis of coagulation factors, and increased fibrinolytic activity, with a slight increase in risk compared to patients without liver disease [13]. However, the vast majority of the procedures in the study, which were performed between 2004 and 2007, were conducted through the femoral artery, the traditional access site due to its direct path to the heart and larger vessel size to accommodate contemporary equipment.

The advent of trans-radial catheterization has provided a safe alternative to undergo percutaneous coronary interventions due to the dual blood supply to the hand from large arteries and the lack of large nerves and veins near the arterial puncture site [14]. Other studies have shown that catheterizations through the radial access site have less bleeding and vascular complications, clear advantages for patient population predisposed to bleeding [15, 16]. In the current study, we performed a retrospective analysis of cardiac catheterizations in ESLD patients from 2004 through 2012, examining the differences in access site complication rates between trans-radial versus trans-femoral catheterizations.

Materials and methods

The study was approved a priori by the University of California San Francisco (UCSF) Committee on Human Research. A retrospective search of the cardiac catheterization database was performed for procedures with the clinical indication of ESLD. We identified 334 patients with ESLD who underwent left heart catheterization and/or concurrent right heart catheterization between August 1, 2004 and December 31, 2012.

The primary predictor variable is categorical (determined by the catheterization access site): femoral or radial. Because one patient had both radial and femoral catheterization attempts, the case was counted in both the femoral and radial groups. Relevant demographic variables include age, gender, weight, blood pressure, heart rate, and baseline laboratory values. Pre-catheterization laboratory values and Model for End-Stage Liver Disease (MELD) scores were selected based on the most recent results prior to the start of catheterization. Procedural variables include sheath size, concurrent right-sided cardiac catheterization, Factor VIIa dose, method of closure and closure device. Factor VIIa dose was measured in the 24 hour timeframe prior to catheterization. Closure devices used were Perclose ProGlide or Starclose (Abbott Medical, Abbott Park, Illinois) or AngioSeal STS (St. Jude Medical, St. Paul, Minnesota). For trans-radial catheterizations, manual compression was used for achieving hemostasis.

Outcome variables are vascular complications, bleeding complications, changes in hemoglobin, hematocrit and INR, and transfusion requirements. Vascular complications include hematoma (> 5 cm), pseudoaneurysm and arteriovenous fistula; bleeding complications include clinically evident intracranial hemorrhage and retroperitoneal bleeding. Post-catheterization hemoglobin and hematocrit were selected based on their lowest values within 48 hours after catheterization or at the time prior to an additional procedure, whichever came first. Transfusions included fresh frozen plasma (FFP), platelets (PLT), and packed red blood cells (pRBCs), and were measured in the 24 hours prior to catheterization to correct for coagulopathy and 24 hours after catheterization because of overt bleeding. Transfusion data for 20 patients between Aug 13, 2004 and June 3, 2005 was lost due to database migration. To identify differences in bleeding outcomes, we compared major bleeding scores and a bleeding index [17, 18].

All data were collected by chart and/or database review. Comparisons between patients who underwent trans-femoral versus trans-radial catheterization were done using Student's t test for continuous variables, Mann-Whitney test for non-parametric continuous variables, and the chi-square test for categorical variables. All statistical tests were 2 sided with an alpha level of 0.05. Multi-variable regression analysis was deferred due to low number of univariate predictors. Analyses were

Table 1. Baseline clinical and angiographic data

Variable	Femoral group (n = 189)	Radial group (n = 145)	*p* Value
Demographics			
Age (yrs)	56.9 ± 8.5	58.6 ± 7.3	0.0558
Female/male	35%/65%	34%/66%	0.8543
Weight (kg)	82.1 ± 21.1	85.3 ± 21.7	0.1892
BMI (kg/m^2)	28.7 ± 6.0	29.2 ± 6.6	0.5536
Diabetes	58%	65%	0.2193
Baseline laboratory values			
Heart rate (beats/min)	73 ± 18	73 ± 22	0.850
Systolic blood pressure (mm Hg)	121 ± 25	96.3 ± 18.2	< 0.0001
Diastolic blood pressure (mm Hg)	64.0 ± 11	55.6 ± 11.2	< 0.0001
Mean blood pressure (mm Hg)	88.0 ± 16	73.0 ± 13.2	< 0.0001
Hemoglobin (g/dL)	11.1 ± 2.02	10.4 ± 1.9	0.001
Hematocrit (%)	32.6 ± 6.0	30.3 ± 5.7	< 0.0006
Platelet count (X 10^9/L)	95.7 ± 67.2	81.5 ± 63.7	0.0517
INR	1.59 ± 0.62	1.94 ± 1.16	0.0001
Serum creatinine (mg/dL)	2.03 ± 1.87	1.87 ± 1.57	0.8215
Creatinine clearance (mL/min)	74.4 ± 46.9	74.4 ± 44.2	0.9997
MELD	21.2 ± 9.2	25.6 ± 10.0	0.0035
Angiographic characteristics			
Sheath size (Fr)			
4	1% (n = 2)	0% (n = 0)	
5	37% (n = 70)	87% (n = 126)	
6	12% (n = 23)	12% (n = 17)	
6.5	47% (n = 88)	1% (n = 1)	
7	1.5% (n = 3)	0% (n = 0)	
8	1.5% (n = 3)	0% (n = 0)	
Concurrent right heart catheterization	69% (n = 130)	46% (n = 67)	< 0.001
Heparin			
Proportion of group received	7.4% (n = 13)	68% (n = 98)	< 0.001
Dose (units)	3300 ± 1300	2800 ± 1500	0.2820
Closure			
Manual	59% (n = 111)	100% (n = 145)	N/A
Angio-Seal	7% (n = 14)	0	N/A
Perclose	24% (n = 46)	0	N/A
Starclose	10% (n = 18)	0	N/A

Data is expressed as mean ± SD or as number (percentage).

performed using Stata version 10 (StataCorp LP, College Station, Texas.).

Results

Demographically, the radial group and the femoral group were not statistically different (**Table 1**). Specifically, typical demographic predictors of bleeding (older age, female gender, and lower weight) were not statistically different between the two groups [19-21]. However, compared to the femoral group, the radial group had laboratory predictors of bleeding pre-procedure: significantly lower blood pressures (systolic, diastolic, and mean; all p < 0.0001), lower hemoglobin (10.4 ± 1.9 versus 11.1 ± 2.02, p = 0.001), hematocrit (30.3 ± 5.7% versus 32.6 ± 6.0%, p < 0.0006), and platelet count (81.5 ± 63.7 versus 95.7 ± 67.2 X 10^9/L, p = 0.0517), and significantly higher INR (1.94 ± 1.16 versus 1.59 ± 0.62, p = 0.0001) (**Table 1**). The radial group was not sig-

Table 2. Comparison of complications between trans-femoral and trans-radial cardiac catheterizations

Complication	Femoral group (n = 189)	Radial group (n = 145)	*p* Value
Any pseudoaneurysm	3.7% (n = 7)	0%	0.0192
Smaller than 2 cm	1.1% (n = 2)	0%	0.2141
Larger than 2 cm	2.6% (n = 5)	0%	0.0485
Any hematoma	3.7% (n = 7)	2.1% (n = 3)	0.3849
Smaller than 5 cm	2.6% (n = 5)	2.1% (n = 3)	0.7327
Larger than 5 cm	1.1% (n = 2)	0%	0.2141
Intracranial bleed	0	0	N/A
Retroperitoneal bleed	0	0	N/A

nificantly different from the femoral group in their serum creatinine and creatinine clearance, also predictors of bleeding [20]. Heparin use was significantly higher in the radial group compared to the femoral group ($p < 0.001$), however heparin dosing was not significantly different between the two groups ($p = 0.2820$; **Table 1**).

The radial group had a lower rate of pseudoaneurysms (0% versus 3.7%, $p = 0.0192$) than the femoral group (**Table 2**). Of the 7 cases of pseudoaneurysms in the femoral group, 6 of the cases required thrombin injection, surgery, or both to fix the pseudoaneurysm. However, there was no statistical difference between the formation of hematomas (2.1% versus 3.7%, $p = 0.3849$) between the radial and femoral groups. There were no cases of arteriovenous fistulas in either group. There was a significantly lower frequency of ultrasound usage used to evaluate possible vascular complications for the radial group compared to the femoral group (0.7% versus 6.9%, $p = 0.0052$).

There were no cases of intracranial or retroperitoneal bleeds in either the radial or the femoral group. There was a significantly lower percentage drop in hematocrit in the radial group compared to the femoral group (5.4% versus 7.8%, $p = 0.0393$). Using a number of different bleeding definitions (**Table 3**), we were unable to demonstrate a statistically significant difference in major bleeding events between the radial and femoral groups. Additionally, there was not a statistical difference between the two groups in bleeding severity ($p = 0.1332$). Pre- or post-catheterization transfusion requirements (platelet, fresh frozen plasma, packed red blood cells) between the radial and femoral group were not significantly different.

We were also interested in clinical predictors of vascular and bleeding complications. While arterial sheath size did not predict any of the major bleeding events mentioned above or bleeding severity, logistic regression analysis showed that increased sheath size corresponded with a significantly higher risk for any pseudoaneurysm (odds ratio [OR] 3.6, 95% confidence interval [CI] of 1.392-9.526; $p = 0.008$). Each increase in sheath size increased the risk of pseudoaneurysm greater than 2 cm (OR = 5.4, 95% CI = 1.7-17.3; $p = 0.003$). If the analysis was limited to the femoral group, there was still a significant increase in risk for pseudoaneurysms greater than 2 cm (OR=3.9, 95% CI = 1.03-14.5; $p = 0.03$). Arterial sheath size predicted TIMI minor bleeding (OR = 2.3, 95% CI = 1.02-4.93; $p = 0.04$). Closure device did not significantly reduce bleeding indices in the femoral group and concurrent right-heart catheterization did not significantly increase chances of bleeding in either group.

Discussion

We compared access site complication rates from cardiac catheterizations between radial and femoral access in ESLD patients to determine the relative safety of trans-radial to trans-femoral procedures. Our cohort included 334 ESLD patients; a search through PubMed demonstrated this is the largest cohort yet in comparing trans-radial and trans-femoral catheterizations in this select patient population. In this study, there was a total complication rate of 2.1% in the radial group and 7.4% in the femoral group. This is comparable with our previous study demonstrating a 12.5% complication rate in catheterizations performed via the femoral artery [13]. Additionally, we also demonstrated a significantly lower rate of pseudoaneurysms in the radial group compared with the femoral group. In general, our lower rate of vascular complications in trans-radial versus trans-femoral catheterizations is consistent with data found in the literature regarding the same procedures in non-ESLD patients [22-24].

Table 3. Comparison of bleeding scores between trans-femoral and trans-radial cardiac catheterizations

Bleeding Definition	Femoral group (n = 189)	Radial group (n = 145)	*p* Value
TIMI Major	4.2% (n = 8)	1.4% (n = 2)	0.1293
TIMI Minor	3.2% (n = 6)	2.1% (n = 4)	0.8250
REPLACE-2 Major	1.1% (n = 2)	1.4% (n = 2)	0.7891
BARC Type 3	3.7% (n = 7)	2.1% (n = 3)	0.3849

Our study did not show a significant difference between the radial and femoral groups in bleeding outcomes or transfusion requirements after catheterization, findings consistent with data from the RIVAL trial which also was unable to demonstrate a statistically significant reduction in major bleeding with radial access [25]. However, other studies have reported trans-radial catheterizations result in lower bleeding risks and less transfusion requirement [16, 26]. While we cannot conclude definitively that radial access in our cohort reduced bleeding, it is interesting to note that there was no increased bleeding outcomes despite higher pre-procedural risks for bleeding in the radial group compared to the femoral group. Furthermore, the radial group had a significantly higher MELD score, suggesting more advanced liver disease and higher risk of bleeding. It may be possible that the innate advantages of radial access (e.g. smaller sheath size, smaller puncture wound, ease of wound compression) reduces some of the bleeding risks associated with compromised liver function. A recent study demonstrated the absence of pseudoaneurysms and a 2% rate of major bleeding (as defined by BARC Type 3) after trans-radial catheterization in their cohort of 82 ESLD patients, findings consistent with ours [27]. Altogether, it appears that cardiac catheterization, femoral or radial, can be performed relatively in ESLD patients, as has also been shown in other studies [28, 29].

We also demonstrated in our study that, though patients who underwent trans-radial catheterizations had a significantly higher INR than those who underwent trans-femoral catheterizations, there were no significant differences between the two groups in bleeding outcomes. This finding is consistent with data reported by Townsend et al [30]. It appears that, while INR can be used as reliable predictor for bleeding in patients without compromised liver function, patients who have cirrhosis are susceptible to either bleeding or thrombosis due to an establishment of a new balance between pro- and anti-coagulant factors [31].

Limitations in this study included the inherent drawbacks of a retrospective study. Also, the patients in the study were not randomized to the femoral or radial groups: a randomized controlled trial may help further elucidate the differences between trans-femoral and trans-radial catheterizations in ESLD patients, particularly regarding bleeding or transfusion requirements and removing operator preference bias. This is a single-center study so our results and conclusions may not be generalizable to the entire ESLD patient population.

Our study addresses a paucity of data comparing the relative safety of invasive cardiac techniques in a patient population highly predisposed to bleeding and vascular complications. In our study, radial access, in patients with ESLD undergoing cardiac catheterization, is associated with lower rates of vascular access site complications and similar rates of bleeding and transfusions compared to femoral access, despite higher baseline bleeding risk.

Disclosure of conflict of interest

Note.

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