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Transradial versus transfemoral arterial access in Yttrium-90 microspheres radioembolization for hepatocellular carcinoma

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ABSTRACT

OBJECTIVE: Transradial access has become more popular in body intervention procedures but has not been ubiquitously adapted. This study assesses the efficacy of this approach in Yttrium-90 labeled microspheres radioembolization. To compare transradial to transfemoral access in hepatocellular carcinoma patients who underwent Yttrium-90 radioembolization.

MATERIALS AND METHODS: A total of 244 hepatocellular carcinoma patients underwent 337 radioembolization procedures at our institute from May 2014 to May 2020. The transradial access-group included 188 patients (252 procedures) while the transfemoral access group had 63 patients (85 procedures). The recovery time, fluoroscopy time, contrast volume, peak radiation dose, and equipment cost for each procedure were all reviewed to evaluate for statistical differences between the two groups.

RESULTS: The transradial cohort recorded a significantly shorter ($P < 0.01$) mean recovery time (from the end of the procedure to discharge) and had a significantly shorter ($P < 0.05$) use of contrast volume versus the transfemoral group. In addition, the radiation dose and fluoroscopy time were lower in the transradial subset, although not statistically different. Furthermore, the overall cost for procedural equipment was significantly less ($P < 0.01$) in the transradial cohort than in the transfemoral. No major complications were reported in the transradial group, while one pseudoaneurysm was noted in the transfemoral group.

CONCLUSION: With respect to many pertinent parameters, transradial access was evaluated as being more advantageous than transfemoral access. The results of this study suggest that transradial access should be considered more often, whenever feasible, as an option in the Yttrium-90 treatment of hepatocellular carcinoma patients.

Keywords: Yttrium-90 microspheres, Radioembolization, Hepatocellular carcinoma

INTRODUCTION

Transarterial radioembolization with Yttrium-90 (Y90) labeled microspheres is considered a valid therapeutic approach to target hepatocellular carcinoma (HCC).[1] For most patients, the treatment is performed via transfemoral artery access (TFA). However, transradial arterial access (TRA) has slowly emerged as an alternative strategy.[2-5]

Namely, the procedure has gained significant traction in body interventional procedures.[2,3,5] Many of these studies have reported numerous advantages of TRA, in concordance with related cardiac intervention research, such as earlier sheath removal, fewer complications, reduced cost, and faster recovery times.[6,7] Additionally, the radial approach has been shown to decrease the risk of entry site complications while also being the preferred route of access for patients in regards to their overall postprocedural comfort.[8-12] Despite this, TRA has been associated with a small yet

significant increase in radiation exposure in both diagnostic and interventional procedures, as well as a higher likelihood of access failure in comparison to TFA.[8-13]

Up to date, there are limited studies in the body interventional literature that compare the transradial and transfemoral access groups in regards to pertinent radiation parameters: recovery time, fluoroscopy time, contrast volume, radiation dose, and procedural cost economics. The purpose of this study is to evaluate the potential benefits and pitfalls between the two different vascular approaches (TRA versus TFA) in the specific population of HCC patients who underwent Yttrium-90 microspheres radioembolization.

MATERIALS AND METHODS

This retrospective study, which was performed under clinical study guidelines, was approved by the institutional review board and determined to be IRB exempt. The demographic information and radiation-related data were collected based on a combination of electronic medical records and radiation safety worksheets for each IR procedure. A total of 244 patients underwent 337 radioembolization procedures at our institute from May 2014 to May 2020. These patients were retrospectively reviewed within two groups: transradial artery approach (188 patients, mean age 62.6 ± 9.74, median age 63 (IQR = 11), total 252 procedures) and transfemoral artery approach (63 patients, mean age 64.7 ± 11.96, median age 65 (IQR = 11.75), total 85 procedures). The choice of procedure was based on the preferences of seven different operators with experience ranging from 2 to more than 20 years of serving as faculty within interventional radiology at a tertiary care hospital. The seven operators all conducted an equal amount of TRA and TFA procedures as one another throughout our study, proving no inconsistencies in training with respect to each subset. All operators also began learning TRA in 2014 with its introduction within our institution. All procedures for both TRA and TFA were conducted in the same up-to-date angiography system (Siemens Healthineers, Malvern, PA).

Transradial artery approach

The completeness of the radio-ulnar palmar arch was evaluated on the left hand of every patient who was considered for radial access using Barbeau's tests.[14] Patients with a type D response were moved to TFA. For every patient, an ultrasound image documented the radial artery to be 2 mm in size. Prior to the procedure, the skin overlying the left radial artery was anesthetized with lidocaine and nitroglycerin paste. Under ultrasound guidance, the radial artery was accessed with a 21-gauge needle. A 0.018-in wire was inserted, the needle was removed, and a 5 French Glidesheath Slender (Terumo, Somerset, NJ) vascular introducer sheath was placed over an 0.021-inch SS microwire (Terumo, Somerset, NJ) without skin incision at the puncture site. For each patient, a radial artery "cocktail" was utilized post-procedure which included 200 ug nitroglycerin, 2.5 mg verapamil, and 3000 units of heparin.

After radioembolization, all wires and catheters were removed. Before removal of the sheath, an arteriogram was conducted to assess for radial artery patency. Following this, a TR Band (Terumo, Somerset, NJ) was placed on the left wrist over the arteriotomy site and inflated to obtain hemostasis. The hemostasis was subsequently maintained for 60 minutes. Arterial hemostasis was reconfirmed as the cuff was incrementally deflated. Upon cuff removal by nursing staff in the recovery unit the patient was observed for an additional 30 minutes prior to discharge.

Transfemoral artery approach

Using ultrasound, the right common femoral artery was accessed with a 21gauge needle and a small skin incision was made at the puncture site. The needle was exchanged for a 5 French transitional micropuncture sheath over an 0.018-in nitinol wire. The micropuncture sheath was then exchanged for a 5 French × 10 cm vascular sheath over a 0.035-in × 145 cm Coons wire.

At the termination of the procedure, an arteriogram was conducted to assess for femoral artery patency. Following this, the catheter and sheath were removed and full hemostasis was achieved by placement of either of the following vascular closure devices: MYNXGRIP (Cardinal Health, Dublin, OH), STARCLOSE (Abbott Vascular, Chicago, IL) or ANGIO-SEAL (Terumo, Somerset, NJ). The patient was then transferred to the recovery area with his/her lower extremity straightened for 2 hours before discharge.

Post-procedure discharge

Repeat evaluation of the access site and pulse (radial or femoral/dorsalis pedis) was performed for all patients before discharge. The follow-up appointment was made based on a future management plan.

Statistical analysis

Patient characteristics were compared between the two groups using the Wilcoxon rank sum test for demographic characteristics.

To evaluate the differences, the data of procedure time (min), fluoroscopy time (min), contrast volume (ml), radiation dose (mGy Peak Skin Dose), and procedural equipment cost ($) were collected for both groups. Wilcoxon rank sum test was used to evaluate for any statistical differences between the two groups. *P*-values of less than 0.05 were considered to be statistically significant. The statistical analysis of results was performed with statistic software (SigmaStat version 2.03, SPSS Inc).

RESULTS

This study noted a total of 244 patients with 188 patients in the TRA group (59.6% under 65 y/o and 76% male), and 63 patients in the TFA group (58.7% under 65 y/o and 71% male). There were no significant differences in terms of age between the two groups [Table 1] ($P > 0.05$ for over and under 65 y/o). The median age of patients was 63 (IQR = 11) years old in the TRA group, and 64.7 (IQR = 11.75) years old in the TFA group. Male was the predominant gender in both groups (76.1% in the TRA group and 71.0% in the TFA group). The recovery time was calculated from the end of the procedure to the time of discharge when the patient could ambulate. There was a significantly shorter recovery time in the TRA group than in the TFA group [Table 2] (Avg = 111.7 min versus 165.6 min, $P < 0.01$).

Fluoroscopy time was automatically calculated by the computer-based on real exposure of X-ray during the radioembolization. There were shorter fluoroscopy times [Table 3] (Avg = 16.1 min versus 19.7 min, $P > 0.05$) in the TRA group than in the TFA group. Accordingly, the contrast volume consumed during radioembolization was significantly less in the TRA group than that of the TFA group [Table 4] (Avg = 69.2 ml versus 75.2 ml, $P < 0.05$).

There was a trend toward lower radiation exposure dose (mGy PSD) in the radial group than in the femoral group, although not statistically significant [Table 3] (Avg = 880.2 mGy versus 995.1 mGy, $P > 0.05$). Notably, the average cost of procedural equipment was significantly cheaper in the TRA group than in the TFA group [Table 2] (Avg = $1632.33 versus $2013.12, $P < 0.01$). Postprocedure recovery evaluation showed no major complications in the TRA group. In the TFA group, one pseudoaneurysm was noted and required further intervention with ultrasound-guided thrombin injection.

DISCUSSION

Much of the literature regarding TRA highlights the myriad of advantages for the procedure. Over the years, TRA has garnered extensive popularity with respect to body interventional procedures.[2,3,5] Most notably, studies point to the TRA approach correlating with earlier sheath removal, fewer complications, reduced costs, faster recovery times, and increased patient preference when compared to TFA.[2,6,7,15] However, in other studies, TRA has shown a small increase in radiation exposure and a higher likelihood of access failure than TFA.[8,13] This investigation compares TRA and TFA in the context of Y90 treatment of HCC, which few studies have done, and finds more noteworthy trends in favor of TRA. In this study, TRA was associated with significantly shorter recovery times, lower usage of contrast volumes, and cheaper procedural equipment cost. TRA also showed lower radiation dose usage and shorter fluoroscopy times versus TFA, although not statistically significant.

All patients within our study underwent mapping angiograms prior to their respective treatment procedures; however, this data was not considered. Mapping data were excluded due to the wide variability in times present in navigating unknown vessels, utilizing cone beam computed tomography for multiple branch vessels, and embolizing non-target branch vessels. Thus, the decision to only include procedural data was mainly done to eliminate confounding parameters and better assess the desired variables (TRA versus TFA) in regard to already known vessels. Additionally, the retrospective nature

Table 1: TRA was accessed with a 21-gauge needle and then a 0.018-in wire was inserted. After needle removal, a 5 French Glidesheath Slender (Terumo, Somerset, NJ) vascular introducer sheath was placed over a 0.021-inch SS microwire (Terumo, Somerset, NJ) without skin incision at the puncture site. All patients with a type D response on the Barbeau's test were excluded from the study. TFA was accessed with a 21gauge needle and then this needle was exchanged for a 5 French transitional micropuncture sheath over an 0.018-in nitinol wire. The micropuncture sheath was then exchanged for a 5 French × 10 cm vascular sheath over a 0.035-in × 145 cm Coons wire. Both accesses were obtained via ultrasound.

Average age and demographics of TRA and TFA cohorts.

Age	TRA	TFA	*P*-value
<65 Y	112 (Median = 58; IQR = 8)	37 (Median = 60.5; IQR = 9)	0.93
≥65 Y	76 (Median = 69; IQR = 8)	26 (Median = 72.5; IQR = 12.75)	0.12
Total #s	188 (Median = 63; IQR = 11)	63 (Median = 65; IQR = 11.75)	

Sex breakdown of TRA and TFA cohorts.

Sex	TRA	TFA
Male	143	45
Female	45	18
Total #s:	188	63

Table 2: Average procedural costs in Y90 radioembolization: TRA versus TFA.

	All (n = 244)	TRA (n = 188)	TFA (n = 63)	*P*-Value
In suite procedure time (min)	124.8	111.7	165.6	<0.01
Material cost (USD)	1822.8	1632.3	2013.1	<0.01

Table 3: Average radiation exposure in Y90 radioembolization: TRA versus TFA.

	All (n = 244)	TRA (n = 188)	TFA (n = 63)	*P*-Value
Peak skin dose (mGy)	909.1	880.2	995.1	0.25
Fluoroscopy time (min)	17.1	16.1	19.7	0.06

Table 4: Average administered contrast volume in Y90 radioembolization: TRA versus TFA.

	All (n = 244)	TRA (n = 188)	TFA (n = 63)	*P*-Value
Contrast (ml)	70.7	69.2	75.2	0.03

of this study partly limited the incorporation of mapping angiograms into the design.

Similar to previous studies, the significantly shorter recovery times noted by TRA in this study are most likely a byproduct of the radial artery being an easier mode of initial access for the operator and faster in achieving hemostasis following the operation. Moreover, increased post-procedural comfort by the patient following TRA also encourages efficient ambulation and discharge which decreases overall recovery time.

In concordance with other investigations, our study documented no complications in the TRA group.[8-10] One pseudoaneurysm was found in the TFA group, which required further ultrasound-guided thrombin injection for treatment. Aside from this, this study's overall complication rate was 1/337 or 0.3%. The increased risk of complications in TFA versus TRA is most likely attributable to the femoral artery being roughly 3× larger in diameter than the radial artery. As one can imagine, the larger the vessel chosen for access the greater risk of complications pertaining to bleeding, AV fistulas, and pseudoaneurysms, among others.

In regards to the rate of access failure, our study did note a higher proportion in the TRA (7/252) than the TFA group (0/252). These seven incidences required the patient to be switched from TRA to TFA. Two of these patients required a change within the procedure due to vasospasm. The other five patients were switched from TRA to TFA given the operators' judgment considering the nature of vessels, the patient's clinical condition, and the relevant patient medical history. All reported data pertaining to these seven patients were inclusive of both access attempts, aside from the procedural cost which was tabulated as the final route of access. These observations, similar to prior studies, underscore the need to consider TFA when TRA is not viable.[8,13]

As aforementioned, the results pertaining to radiation exposure, fluoroscopy time, and contrast volume are quite noteworthy in this study. The trend toward decreased radiation dose is particularly interesting because it is in contrast with existing TRA literature, which mainly focuses on cardiac procedures. A potential explanation for the decreased radiation dose observed in Y90 TRA versus Y90 TFA centers on the direction of the catheter in relation to normal blood flow. In Y90, the TRA catheter follows the body's natural current of blood by being advanced down the descending aorta. Meanwhile, the TRA catheter in cardiac procedures is advanced against the flow of the ascending aorta which inevitably extends procedural time and subsequent radiation usage. This also helps explain why Y90 TFA necessitates higher radiation doses and longer procedure times because the catheter is being advanced up against the normal downstream flow of the femoral artery. These differences are further accentuated in favor of TRA with increased operator comfort and experience with this technique. Similarly, the trend in fluoroscopy dose can be explained as a byproduct of the time associated with the procedure and the subsequent need for radiation. Further research is needed to explain potential reasoning for the trend in lower contrast volumes for TRA, as the authors are unable to delineate one within this study's current setup.

The final variable assessed in our study was procedural equipment cost between TRA and TFA subsets. Cost analysis did not include each patient's post-procedure hospital cost but rather was confined to the charges associated with items (i.e., catheters, guide wires, and syringes) used within the duration of the procedure. The cost of the angiography suite time was not built into this model. Based on our data, TRA was approximately $380 cheaper than TFA per operation, translating to a net savings of $21,340/year across 56 HCC

Y90 procedures conducted at our institution. A portion of this cost disparity can be attributed to the closure devices used in both procedures. The STARCLOSE, MYNXGRIP, or ANGIO-SEAL closure devices recommended in our TFA are roughly $200 more than the TR Band utilized in TRA. Given our tremendously high patient volume, this institution prefers TFA closure devices as opposed to manual compression and compression due to its greater convenience for the operator, increased comfort for the patient, and higher efficiency at achieving effective hemostasis, allowing for maximal patient turnaround. This study's reported TRA savings are underestimated because our data do not account for the additional post-procedural monetary benefits. According to one systematic review, TRA was reported to save hospitals, on average, $275 more per patient versus TFA when factoring in additional parameters such as hemostasis time and the inpatient hospital cost related to procedural complications.[16] These observations only further bolster our institution's findings to suggest that TRA is more cost efficacious than TFA.

Several limitations of this study center on its retrospective nature, and also its assessment from a single institution's perspective. Despite the statistically significant trends found in favor of TRA, there were undeniably a greater number of patients in the radial access-group than the femoral one. This observation partially explains the slightly higher male percentage in TRA over the TFA group which is an artifact of mostly males living within our study's location and receiving medical care from our institution. The predominance of TRA within our institution starting from its advent in 2014, and its gradual preference over time has also contributed to the discrepancy of sampling in this study. The operators of this study favored TRA due to its easier mode of access, greater visible patient satisfaction, and faster observed recovery times following procedures. Based on literature and prior clinical experience, this study's investigators preferred TRA over TFA due to decreased complication risks in regard to AV fistulas and pseudoaneurysms. Generally, TFA was reserved for cases where vessels displayed extreme tortuosity, and where navigation of the aortic arch or radial artery proved quite difficult. In addition, all patients who showcased a type D response in the Barbeau's test or had a high risk for radial artery vasospasm were moved to TFA instead. Further adding to the complexity of TFA cases, patients with prior unsuccessful TRA attempts, or who had notable coagulopathic considerations and bleeding risks were considered for TFA. Given this study's retrospective nature, this heavy utilization of TRA was unable to be appropriately accounted for. As a result, randomized controlled trials would help mitigate any biases in regard to TRA utilization, allowing further confirmation of this study's results.

Everything considered, patients in this study who underwent Y90 radioembolization via TRA had significantly faster recovery times and were administered significantly lower contrast volumes. TRA was also significantly less expensive than TFA and noted trends lower in both fluoroscopy time and radiation dose. No major complications were noted in the radial group while one pseudoaneurysm was found in the femoral group. The results of this investigation suggest that when feasible TRA should be strongly considered in the Y90 radioembolization of HCC patients.

Declaration of patient's consent

Institutional Review Board (IRB) permission was obtained for the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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