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ORIGINAL PAPER

Transradial left ventricular endomyocardial biopsy: assessment of safety and efficacy

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Abstract
Background We aimed at assessing the safety and efficacy of a systematic transradial approach for left ventricular endomyocardial biopsy using a new hydrophilic sheathless guiding catheter.
Methods and results Forty-two consecutive patients were included. The transradial success rate was 98 % (41 of 42). In one case, cross over to femoral access due to irreversible spasm of the right radial artery was necessary. No radial spasm was observed in the other 41 patients. Depending on the indication, several other procedures, such as coronary angiography or ventricular angiography, were additionally performed through the same transradial access site. Median fluoroscopy time was 7.9 min. The mean dose area product was 1867 cGy × cm^2. All biopsy samples were graded as good or excellent quality. No patient had any complications. Immediate post-procedural ambulation could be achieved in all patients. Radial artery patency was confirmed by duplex sonography 24 h after removal of the guide.
Conclusion The present study demonstrates safety and efficacy of a systematic transradial access for left ventricular EMB using a highly hydrophilic sheathless guiding catheter. This is of clinical importance since this new technique may overcome critical limitations of the common approach.

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Keywords Transradial access · Transfemoral access · Endomyocardial biopsy · Complications · Sheathless guiding catheter · Left ventricular biopsy · Myocardial disease

Abbreviations

ACH	Intracoronary acetylcholine testing
CA	Coronary angiography
EMB	Endomyocardial biopsy
FFR	Fractional flow reserve
LVA	Left ventricular angiogram
LV	Left ventricle
LV-EF	Left ventricular ejection fraction
PCI	Percutaneous coronary angioplasty
RHC	Right heart catheterization
RV	Right ventricle
TRA	Transradial access

Introduction

Endomyocardial biopsy is the current gold standard for work-up of non-ischemic myocardial disease [1–5]. As a recent analysis of 755 procedures and 6371 biopsy samples demonstrated that LV-EMB is associated with a significantly lower procedural risk, while yielding similar results as RV or biventricular EMB [6], isolated LV-EMB seems to be the strategy of choice if EMB work-up is needed. However, for this strategy, transarterial access is required. The commonly used transfemoral access is associated with bleeding from the access site due to the need for large diameter sheaths, and needs strict post-procedural immobilization. Thus, a current joint scientific statement of

the American Heart Association, the American College of Cardiology, and the European Society of Cardiology concluded that newer interventional techniques are desirable to improve the safety and efficacy of EMB [7].

Arterial access via the radial artery is increasingly used for diagnostic coronary angiography and percutaneous coronary interventions. It is associated with fewer vascular access site complications, and has been shown to reduce major bleeding when compared to the femoral approach [8–10]. While, being accepted as an equal alternative for coronary interventions, it is still believed to be restricted to this field due to the limited capability of the radial artery to bear large diameter guiding catheters such as needed for EMB. Thus, our aim was to provide a first safety and efficacy assessment for a systematic transradial approach for left ventricular EMB using a new highly hydrophilic sheathless guiding catheter [11].

Methods

Patient population

From March 2012 to September 2014, all patients presenting to our outpatient clinic for EMB work-up of myocardial disease were screened for EMB via transradial access using a modified Allen Test ($n = 74$, see Fig. 1). In total $n = 42$ consecutive patients with normal Allen Test gave informed consent for transradial biopsy, and were included in the study (Fig. 1). In the first patients duplex sonography of the radial arteries was additionally performed before EMB to rule out vascular malformations. Further information on the patient population is given in Table 1.

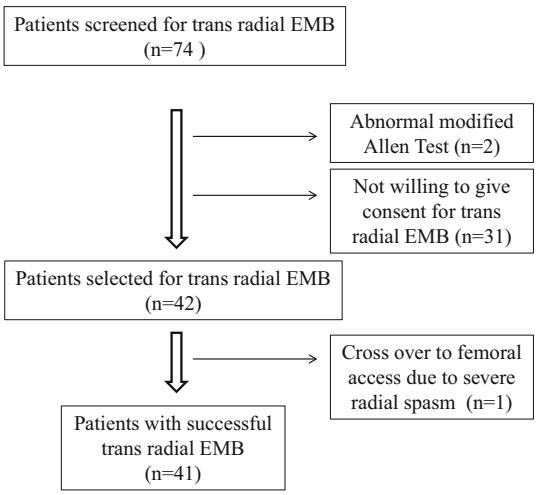

Fig. 1 Patient screening and inclusion flow-chart of the present study

Table 1 Clinical characteristics

		N or quartiles	Range
All patients (*n*)		42	
Age (years)	56	48, 65	27, 80
Height (cm)	173	168, 180	158, 189
Weight (kg)	88	66, 104	49, 150
BMI (kg/m^2)	29.03	24, 33	19, 46
Female (%)	31	13	
NYHA class (%)			
NYHA I	12	5	
NYHA II	19	8	
NYHA III	52	22	
NYHA IV	17	7	
Coronary artery disease (%)	76	32	
Anticoagulation (%)			
Anti-platelet	40	17	
Oral anti coagulant	26	11	
Blood work			
INR	1.15	1.02, 1.21	1.00, 1.75
CREA (mg/dl)	1.09	0.83, 1.10	0.6, 3.4
PLT (GIGA/l)	215	186, 235	108, 436
Functional parameters			
EF (%)	34	25, 45	9, 76
EDV (ml)	241	180, 282	77, 393
LVEDD (mm)	49	31, 66	7, 80
LVEDP (mmHg)	23	15, 30	8, 50

BMI Body Mass Index, *NYHA* New York Heart Association Functional Class, *EF* ejection fraction in %, *LVEDV* left ventricular end-diastolic volume in ml, *LVEDD* left ventricular end-diastolic diameter in mm, *LVEDP* left ventricular end-diastolic pressure in mmHG, *INR* International Normalized Ratio, *CREA* creatinine in mg/dl, *PLT* thrombocyte count in GIGA/l

Transradial coronary angiography and right heart catheterization

All procedures were performed by experienced interventional cardiologists used to work with transradial access on a regular basis. Where clinically indicated, right heart catheterization was performed using an appropriate vein of either the right or the left arm as described elsewhere [1–12]. Left heart catheterization was performed via the right radial artery using a routine transradial access protocol. In brief, after local anesthesia with 2 ml of 0.1 % Mecaine a dedicated 5F transradial sheath was introduced into the right radial artery. Verapamil (2.5 mg) and nitroglycerin (0.2 ml) were administered prior to catheter insertion to prevent radial spasm. Subjects received 5000 units of unfractioned heparin and coronary angiography was performed using either dedicated transradial catheters (TIGER® I or II, Terumo, Tokyo, Japan) or standard

Judkins left or right curves. If microvascular or epicardial coronary spasm was considered as a differential diagnosis, an additional coronary acetylcholine test was performed [13].

Radial EMB procedure

With no dedicated material for transradial EMB, we first reviewed the equipment available. The 7F sheath routinely used at our institution has an outer diameter of 3.1 mm which is generally regarded as too large for radial access, at least if applied to a majority of individuals. Thus, we decided to use large bore sheathless guiding catheters (EauCath®, ASAHI Intec, Tokyo, Japan). These guiding catheters in the 7.5F configuration offer a large inner diameter of 2.057 mm while featuring an outer diameter of just 2.50 mm, which is equivalent to the outer diameter of a standard 6F sheath introducer (Fig. 2). This inner diameter provides the option to position a large variety of biotomes in the LV. For the majority of patients, we used this 7.5F EauCath sheathless guide in combination with a 5.4F bioptome (Maslanka Cardiobioptome, Maslanka, Tuttlingen Germany) with an overall outer diameter of 1.8 mm for all (Fig. 3) except the first three patients, in whom we used an 8.5F EauCath sheathless guide in combination with the institutional standard Meiners Bioptome (Meiners Medizintechnik GmbH, Monheim, Germany).

An MP2 curve was used in the first case, whereas for the following procedures the MP1 was chosen, since it turned out to be the more suitable curve. For all types, the guiding catheter was inserted over a 0.035″ angiographic wire. The sheathless EauCath catheters require a dilator during insertion to reduce the gap between the guide wire and the catheter, since it requires a certain degree of stiffness to insert the catheter into the body where the dilator takes an active role. Given the rather sharp end of the dilator, unlike for standard transradial procedures, the guide was continuously advanced under fluoroscopic control until the tip of the inlet reached the ascending aorta. The inlet was removed over a regular guide wire and replaced by a 6F standard pigtail catheter for crossing of the aortic valve. Once in the LV cavity, the pigtail catheter was removed and the position of the guide pointing towards the free LV was confirmed in two planes (RAO 35° and LAO 60°). A standard Y-shaped hemostasis valve was connected to the guide and the system was thoroughly flushed with saline after connection to the standard institutional angiography manifold (Fig. 4).

The guide wire was then replaced by the bioptome. Under subsequent fluoroscopic control up to ten biopsy samples were obtained from different locations of the LV. During the procedure, air aspiration was carefully avoided by repetitive back bleeding and manual flushing. Finally, the initial angiographic wire replaced the bioptome, and with the guide still in place a standard compression device (TR-Band®, TERUMO) was placed over the access site and inflated with 12 ml air. The guide could then easily be removed while instant hemostasis was achieved. Patients

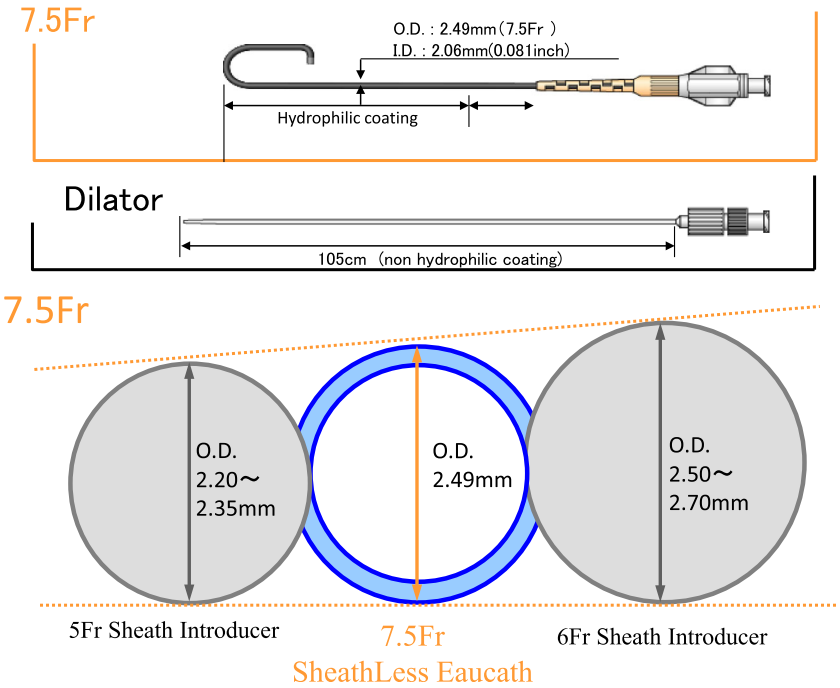

Fig. 2 Comparison of the outer diameter of the Asahi EauCath® Sheathless Guiding Catheter with a standard sheath introducer. Note that the inner diameter of the EauCath® Sheathless Guiding Catheter compares to a larger standard sheath introducer, see text for details

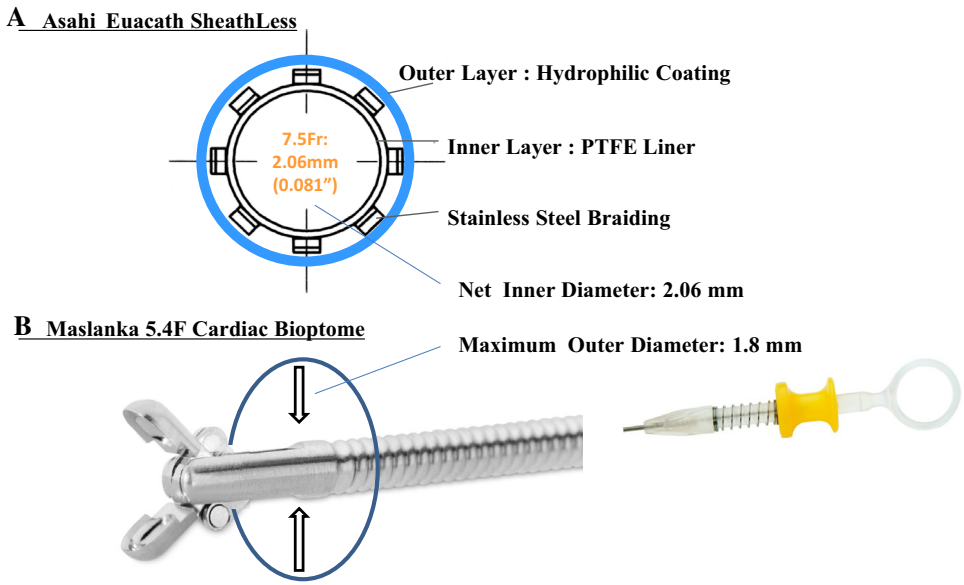

Fig. 3 Comparison of the inner diameter of the EauCath® Sheathless Guiding Catheter with the outer diameter of 5.4F Maslanka Cardiac Bioptome

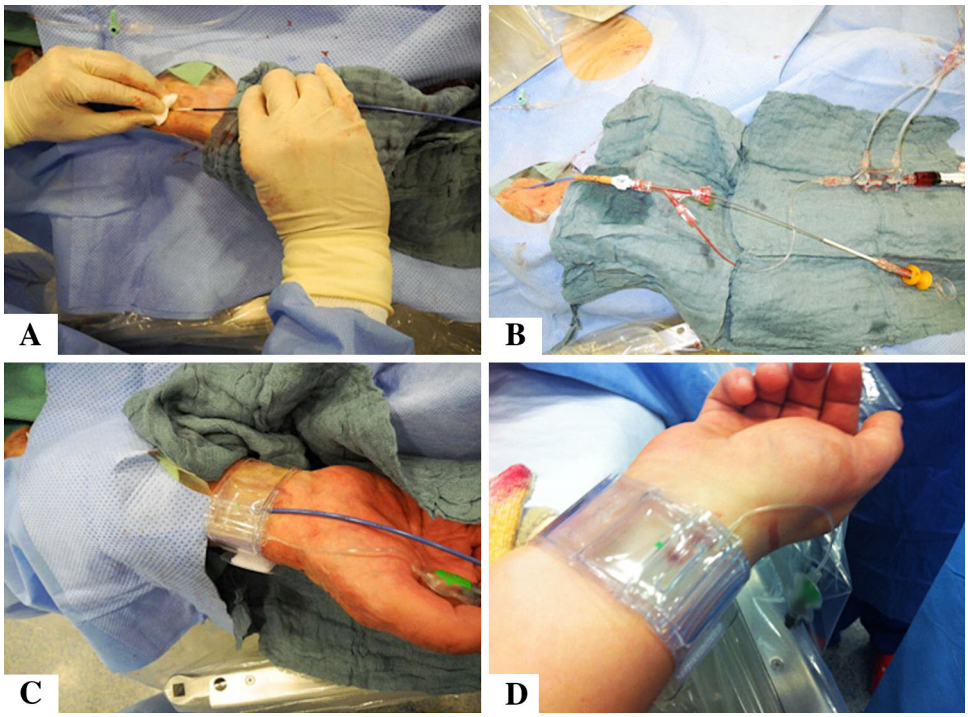

Fig. 4 **a** Demonstrates the introduction of the Sheathless Guiding Catheter into the right radial artery. An overview of the typical setup for transradial EMB, including the guide, the Y-shaped hemostatic valve, the angiography manifold, as well as the bioptome is provided in **b**. **c** Depicts the removal of the guide with the inflated standard compression device already in place. After removal of the guide instant hemostasis is achieved, as shown in **d**. See text for additional details

routinely received immediate bedside echocardiography to rule out pericardial effusion. Radial patency was assured by duplex sonography 24 h after the procedure.

Data analysis and statistics

Safety and efficacy parameters were: (1) procedural success, (2) quality of biopsy samples as assessed by participating pathologists, (3) radiation exposure, (4) procedural time, (5) time to ambulation, (6) access site vessel patency, and (7) relevant access site complications (defined as: false aneurysm, AV-fistula, drop in hemoglobin of more than two points without pericardial effusion or other overt bleeding requiring action, indication for bed rest due to the procedure).

Since the objectives of this safety and efficacy evaluation are descriptive in nature, no formal hypothesis testing was done. Absolute numbers and percentages were computed to describe the patient population. Medians (with quartiles) or means (with standard deviation) were

computed as appropriate. All statistical analyses were performed using the SAS© statistical package, version 9.2 (SAS, Cary, North Carolina).

Results

Patient population

Mean age was 56 years and 31 % of patients where female. The mean BMI of 29 kg/m^2 reflects relevant over weight in our patient cohort. Most patients had moderately or severely impaired LV-EF (median 34 %). At the time of the procedure, 40 % of patients where on anti-platelet therapy, and 26 % where treated with some form of oral anticoagulation. Whereas anti-platelet medication was continued, oral anticoagulation was stopped and the INR had to be <2.0 before the transradial invasive procedure. The median INR was 1.15, ranging from 1.0 to 1.75, with a median platelet count of 215 GIGA/l, ranging from 108 to 436 GIGA/l. Additional patient characteristics can be viewed in Table 1.

Procedural characteristics, safety and efficacy

Depending on the clinical indication, the transradial invasive evaluation encompassed the whole spectrum from EMB as a standalone procedure, combined left/right heart catheterization, or even PCI following FFR. To rule out functional coronary or micro vascular disease as an underlying cause for LV dysfunction, an additional intracoronary acetylcholine test was performed in 13 individuals.

In one case, there was a need to cross over to femoral access due to irreversible spasm of the right radial artery after administration of local anesthesia, while no further case of radial spasm was observed. Thus, the success rate of EMB via transradial access was 98 % (41 of 42) in our population. Table 2 provides a detailed overview of the different procedures performed during the invasive evaluation, as well as the final diagnosis obtained by EMB.

The median duration of the invasive evaluation was 44 min (range 20–86 min), including all procedures performed in one individual. The mean amount of contrast media used was 120 ml per patient, ranging from 20 to 350 ml, also depending on the procedures performed (Table 2). The number of biopsy samples harvested depended on operators' discretion but was not less than six in any patient and 8.4 samples were obtained per patient in average. All biopsy samples harvested via transradial access where graded as good or excellent quality by the pathologists involved. We did not obtain any biopsy sample that was not diagnostic. No patient had access site-, or any other complications as specified before. Immediate post-procedural ambulation could be achieved in all patients independent of the procedures performed, as for no patient any bed rest was assumed necessary.

Overall mean fluoroscopy time was 7.9 min ranging from 2 to 26 min, depending on the procedures performed (Table 3; Fig. 5). The median dose area product was 1867 cGy × cm^2, with a median skin dose of 607 mGy. All patients had patent radial arteries 24 h after removal of the guide confirmed by duplex sonography.

Discussion

The present study demonstrates safety and efficacy of a systematic transradial approach for left ventricular EMB. This is of clinical importance since the new transradial technique may overcome limitations of the commonly used femoral approach, such as bleeding form the access site due to the need for large diameter sheaths, or strict post-procedural immobilization. Therefore, LV-EMB via transradial access may be the new interventional technique of choice, improving the safety of EMB [7].

Patient population

Age, gender, and body mass index distribution in our patient population (Table 1) was in line with many other study populations presenting for the work-up of heart failure in the western world [14, 15]. This also holds true for the mean left ventricular function and other functional parameters [15, 16] (Table 1). Oral anticoagulation, which is frequently indicated in heart failure patients, was stopped before invasive evaluation. However, all invasive procedures were performed up to an INR of 2.0, making the management of patients on oral anticoagulation easier, nicely underscoring the advantages of the transradial access [8, 9, 17].

Procedural characteristics, safety and efficacy

Procedures encompassed the whole spectrum ranging from EMB as a standalone procedure, or combined left/right heart catheterization to PCI following FFR measurement, reflecting the potential of the transradial approach (Fig. 5). Consequently, transradial access may be regarded as an interventional "one stop shop" technique.

The success rate in our population was 98 % (41 of 42). In one patient, we had to cross over to femoral access due to irreversible spasm of the right radial artery after administration of local anesthesia. Despite the fact that the incidence of radial spasm greatly varies in literature [18], our cross over rate nicely matches other reports of transradial interventions [17]. Importantly, the use of the

Table 2 Overview of procedures performed and final diagnosis

Patient	Success	LV-angiogram	Coronary angiography	EMB	PCI	RHC	Renal artery angiography	ACH	Procedural time (Minutes)	Contrast (ml)	No. of biopsy samples	Final diagnosis by EMB
1	Yes	No	Yes	Yes	No	No	No	No	27	40	6	Myocarditis
2	Yes	No	Yes	Yes	No	Yes	No	Yes	65	230	7	Myocarditis
3	Yes	No	Yes	Yes	No	Yes	No	Yes	65	150	6	DCM
4	No	–	–	–	–	–	–	–	–	–	–	–
5	Yes	Yes	Yes	Yes	No	Yes	No	Yes	51	160	8	Myocarditis
6	Yes	No	Yes	Yes	No	Yes	No	Yes	57	180	8	DCM
7	Yes	No	Yes	Yes	No	No	No	Yes	46	140	10	Myocarditis
8	Yes	No	Yes	Yes	No	No	No	No	42	70	8	DCM
9	Yes	No	No	Yes	No	No	No	No	24	20	10	DCM
10	Yes	No	No	Yes	No	Yes	No	No	37	50	12	DCM
11	Yes	No	Yes	Yes	No	No	No	No	20	100	10	Amyloidosis
12	Yes	Yes	Yes	Yes	No	No	No	Yes	86	155	10	Myocarditis
13	Yes	No	No	Yes	No	Yes	No	No	54	50	8	Amyloidosis
14	Yes	No	Yes	Yes	No	No	No	No	27	80	11	Hypertensive CMP
15	Yes	No	Yes	Yes	No	No	No	Yes	41	170	10	DCM
16	Yes	No	Yes	Yes	No	Yes	No	No	41	180	9	HCM
17	Yes	No	Yes	Yes	No	Yes	No	No	44	120	6	DCM
18	Yes	No	No	Yes	No	No	No	No	22	60	8	Myocarditis
19	Yes	No	Yes	Yes	No	Yes	No	Yes	67	200	6	DCM
20	Yes	No	Yes	Yes	No	No	No	No	21	20	8	DCM
21	Yes	Yes	Yes	Yes	No	Yes	No	No	48	120	8	Myocarditis
22	Yes	No	Yes	Yes	No	No	No	Yes	65	190	10	HCM
23	Yes	No	Yes	Yes	No	No	No	No	19	70	10	Myocarditis
24	Yes	No	Yes	Yes	No	No	No	No	31	60	9	Myocarditis
25	Yes	Yes	Yes	Yes	No	Yes	No	No	80	210	7	DCM
26	Yes	No	Yes	Yes	No	No	No	No	39	80	6	Myocarditis
27	Yes	No	Yes	Yes	No	Yes	No	No	50	120	7	DCM
28	Yes	No	No	Yes	No	No	No	Yes	24	200	10	Non compaction
29	Yes	No	Yes	Yes	No	No	No	Yes	43	140	12	DCM
30	Yes	No	Yes	Yes	Yes	Yes	No	No	81	100	6	Amyloidosis
31	Yes	No	Yes	Yes	No	Yes	No	Yes	65	150	8	DCM
32	Yes	Yes	Yes	Yes	No	No	No	No	50	150	10	DCM
33	Yes	No	No	Yes	No	No	No	No	55	350	6	Myocarditis
34	Yes	No	Yes	Yes	No	No	Yes	No	40	100	10	HCM
35	Yes	Yes	Yes	Yes	No	No	No	No	56	100	6	Toxic CMP
36	Yes	No	Yes	Yes	No	Yes	No	Yes	84	90	10	Myocarditis
37	Yes	Yes	Yes	Yes	No	No	No	No	35	100	8	Hypertensive CMP
38	Yes	No	Yes	Yes	No	No	No	No	44	100	7	DCM
39	Yes	No	Yes	Yes	No	No	No	No	53	50	8	Hypertensive CMP
40	Yes	No	Yes	Yes	No	No	No	No	35	60	10	Myocarditis
41	Yes	No	Yes	Yes	No	No	No	No	32	50	10	Amyloidosis
42	Yes	No	Yes	Yes	No	No	No	No	47	180	10	Myocarditis

LV-Angiogram laevocardiography, *EMB* endomyocardial biopsy, *PCI* percutaneous coronary intervention, *RHC* right heart catheterization, *ACH* intracoronary acetylcholine provocation testing, *DCM* dilated cardiomyopathy, *HCM* hypertrophic cardiomyopathy, *Toxic CMP* post chemotherapy toxic cardiomyopathy

Table 3 Efficacy and safety parameters

Patient	Biopsy quality	Total fluoroscopy time (minutes)	Dose area product (cGy cm^2)	Total skin dose (mGy)	Immediate mobilization (yes/no)	Complications (yes/no)	Radial artery patency 24 h (yes/no)
1	Excellent	3	170	40	Yes	No	Yes
2	Excellent	12	6249	1023	Yes	No	Yes
3	Excellent	12	7645	3371	Yes	No	Yes
4	–	–	–	–	–	–	–
5	Excellent	8	875	164	Yes	No	Yes
6	Excellent	10	6917	2142	Yes	No	Yes
7	Excellent	7	2691	927	Yes	No	Yes
8	Excellent	11	2919	464	Yes	No	Yes
9	Excellent	5	1033	130	Yes	No	Yes
10	Excellent	8	403	72	Yes	No	Yes
11	Excellent	4	1176	285	Yes	No	Yes
12	Excellent	12	1198	261	Yes	No	Yes
13	Excellent	6	175	19	Yes	No	Yes
14	Excellent	5	1273	306	Yes	No	Yes
15	Excellent	8	3493	1300	Yes	No	Yes
16	Excellent	6	1150	233	Yes	No	Yes
17	Good	9	4748	886	Yes	No	Yes
18	Excellent	5	1118	178	Yes	No	Yes
19	Excellent	13	2663	607	Yes	No	Yes
20	Excellent	3	772	315	Yes	No	Yes
21	Excellent	7	3558	1031	Yes	No	Yes
22	Excellent	8	2470	719	Yes	No	Yes
23	Good	4	3291	860	Yes	No	Yes
24	Excellent	4	1395	682	Yes	No	Yes
25	Excellent	26	9507	1066	Yes	No	Yes
26	Excellent	9	798	111	Yes	No	Yes
27	Excellent	12	4726	830	Yes	No	Yes
28	Excellent	6	962	109	Yes	No	Yes
29	Excellent	6	1676	830	Yes	No	Yes
30	Excellent	11	3169	736	Yes	No	Yes
31	Excellent	7	3464	1135	Yes	No	Yes
32	Excellent	8	1867	378	Yes	No	Yes
33	Good	4	710	73	Yes	No	Yes
34	Good	9	4825	935	Yes	No	Yes
35	Good	4	363	192	Yes	No	Yes
36	Excellent	12	1340	320	Yes	No	Yes
37	Excellent	10	4250	834	Yes	No	Yes
38	Good	8	6384	1447	Yes	No	Yes
39	Excellent	4	2704	784	Yes	No	Yes
40	Excellent	5	828	183	Yes	No	Yes
41	Excellent	4	835	257	Yes	No	Yes
42	Excellent	10	4321	1330	Yes	No	Yes

sheathless guiding catheter along with a matching bioptome did not result in any radial spasm in all 41 patients undergoing EMB. The procedural time and the amount of contrast agent used (Table 2) depended on the procedures performed in each individual patient, and were very acceptable compared to other datasets [19].

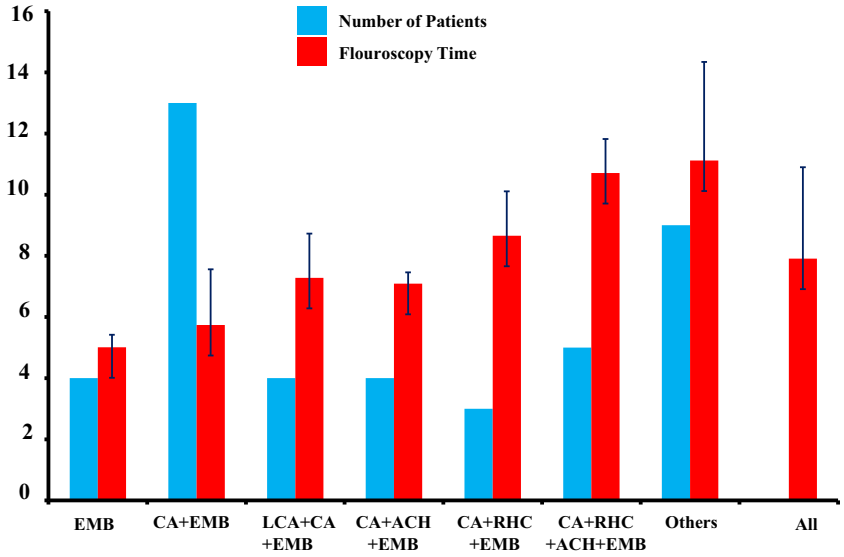

Fig. 5 Detailed distribution and respective fluoroscopy times for all different combinations of invasive procedures performed in this study. All values expressed in minutes as median and quartiles. Note the dependence of the fluoroscopy time on the invasive procedures performed in the individual patient

According to our pathologists, the quality of the biopsy specimens was good or excellent (Table 3), allowing complete work-up of EMB from all patients regarding histology, immunohistology and molecular pathology (infections). Despite a mean BMI of 29 kg/m^2, a maximum INR of up to 1.75, and 40 % of patients being on antiplatelet medication, we did not experience any bleeding or other access site complication, also underscoring the advantages of the transradial approach. After exclusion of pericardial effusion by bedside echocardiography, all patients could immediately be mobilized, which may significantly reduce the length of hospital stay required, possibly offering a considerable economic benefit [20]. Fluoroscopy time and radiation dose (Table 3) were also dependent on the procedures performed, and compare well with other interventional datasets [19, 21].

Another frequent concern raised with regard to transradial procedures is the access vessel patency, potentially limiting multiple accesses [22]. However, in our sample, all access vessels were confirmed patent by duplex sonography 24 h after removal of the guide.

Clinical implications

A procedure combining the advantages of LV-EMB [6] with the benefits of transradial access [8, 9, 17] seems very desirable for the clinical routine. Consequently, the present study may serve as a blueprint for operators willing to perform transradial EMB with its unquestionable advantages. However, in the current study, we did not have a randomized control group allowing direct comparison of procedural parameters and results to the standard femoral approach. In addition, there is an obvious heterogeneity among the procedures performed in our population, reflecting the needs of a real world clinical routine setting. A prospective randomized trial could further investigate the advantages of the transradial approach for LV-EMB.

Conclusion

The present study demonstrates safety and efficacy of a systematic transradial access for left ventricular EMB using a highly hydrophilic sheathless guiding catheter. This is of clinical importance since with transradial biopsy bleeding is less likely than by the transfemoral approach and immediate patient ambulation can be achieved.

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