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ORIGINAL ARTICLE

Variation in Anticoagulation Practices in the Congenital Cardiac Catheterization Lab: Results of a Multinational PICES Survey

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Abstract

The complex nature of congenital heart disease (CHD) has hindered the establishment of management standards for peri-catheterization anticoagulation. We sought to describe anticoagulation practice variability among providers performing cardiac catheterization in children and adults with CHD. A web-based survey (http://www.surveymonkey.com) was distributed to pediatric and congenital interventional cardiologists. Respondents were queried on their training, practice setting, years in practice, and case volume. Clinical questions focused on general anticoagulation strategies and on five common clinical scenarios: two diagnostic (biventricular circulation, single ventricle physiology) and three interventional cardiac catheterizations (atrial septal defect closure, pulmonary artery stenting in Fontan circulation, stent placement for coarctation of aorta). Seventy-seven pediatric and congenital interventional cardiologists responded to the survey (81% in the United States). Twenty-six (36%) worked in a public medical institution; 57% worked in a free-standing children's hospital. Twenty-six percent had been in practice for < 5 years and 32% for > 15 years; 75% completed additional training in interventional congenital cardiology. The median number of cases performed was 200/year (IQR 110); median number of interventional cases was 100/year (IQR 100). Responses to general queries and specific clinical scenarios suggested significant variation in anticoagulation practices, including monitoring of anticoagulation during catheterization, protamine use, and outpatient anticoagulation after catheterization. Practices not only varied between providers but also between different clinical scenarios. Practice patterns did not correlate with provider experience or case volume. Management of anticoagulation in the congenital cardiac catheterization lab varies from operator to operator. Our study may provide some initial insight and context for discussion regarding anticoagulation in a field of increasingly heterogeneous interventional techniques and patient substrates. Future studies would be helpful to better define "best practices" for peri-procedural thromboprophylaxis in patients with congenital heart disease.

Keywords Survey · Cardiac catheterization · Anticoagulation · Quality improvement

Background

Cardiac catheterization in children with congenital heart disease incorporates a broad spectrum of anatomic and pathophysiologic considerations. In addition, patients treated in a congenital cardiac catheterization lab may range in size from very small pre-term neonates to full grown adults. This demographic heterogeneity inevitably results in differences in how congenital cardiac catheterizations are conducted from operator to operator and from institution to institution. Thus, defining practice patterns in the care of patients with congenital heart disease can be difficult. Online surveys and retrospective analysis of registry data have both been used to define practice variability, each approach with its own limitations [1, 2].

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Bleeding and thrombosis complications are among the adverse events most frequently encountered during cardiac catheterization of children and adults with congenital heart disease [3–5]. Defining the variations in practice related to the management of thromboprophylaxis and hemostasis is necessary to identify opportunities for quality improvement. The purposes of this study are to describe current practice patterns regarding anticoagulation before, during, and after congenital cardiac catheterization.

Methods

A 59-question online survey (surveymonkey.com) was distributed by the Pediatric Interventional Cardiology Early Career Society (PICES) to interventional pediatric cardiologists via email listservs for the Congenital Cardiovascular Interventional Study Consortium (CCISC) and the Congenital Heart Disease (CHD) Council of the Society for Cardiovascular Angiography and Intervention (SCAI). Multiple email invitations were sent to maximize the number of respondents. Demographic data, including formal training, time since training, and current work environment were collected. Because of overlap between CCISC and CHD Council memberships, survey responses were reviewed for uniqueness based upon demographic data to ensure that no duplicate responses were included.

Respondents were first asked about their general preprocedural approach to patients who receive anti-coagulation or anti-platelet therapy prior to routine hemodynamic cardiac catheterization (Online Appendix). They were next presented with five specific clinical scenarios: two simple, non-interventional cases (Scenarios 1 and 2), and three interventional cases (Scenarios 3, 4, and 5) (Table 1). Each clinical scenario was followed by a series of questions designed to assess their general approach to anticoagulation during and after certain congenital catheterization procedures. Non-interventional scenarios focused on the following: heparin administration during the procedure, frequency of monitoring of activated clotting time (ACT), the use of protamine for heparin reversal, strategies for prevention of pulse loss. Interventional scenarios focused on: heparin administration during the procedure, frequency of ACT monitoring, use of protamine, and post-procedural recommendations for anti-platelet or anti-coagulation therapy. For Scenarios 1 and 2, respondents were first asked whether they would routinely anticoagulate the patient at the beginning of the procedure after obtaining vascular access. They were then asked about the initial dose of heparin that they would administer. For Scenarios, 3–5 anticoagulation was assumed, and respondents were only queried regarding initial heparin dosing. Only those respondents who acknowledged performing the intervention presented in the clinical scenario at least once per year on average were permitted to answer questions for that scenario. This threshold of performing an intervention at least once per year was selected to allow consistency between each scenario, while capturing a broad response for the scenarios involving both common (e.g., ASD closure) and less common procedures (e.g., Fontan stent implantation).

Statistical Analysis

Multiple-choice response data are presented as percentages. Continuous data are presented as median range. When there was general variability in described practice, responses were compared to demographic data using logistic regression analysis. P values < 0.05 were considered statistically significant.

Table 1 Clinical scenarios

Scenario 1	You are performing a routine, hemodynamic antegrade right, and retrograde left heart catheterization on a 6 month-old, 8 kg infant with a history of repair of complete AV canal. Vascular access includes a 3.3 French femoral artery sheath and a 5 French femoral vein sheath.
Scenario 2	You are performing a routine "pre-Glenn" hemodynamic catheterization on a 4 month-old, 6 kg infant with pulmonary atresia, and intact ventricular septum who is S/P modified right BT shunt placement with a 3.5 mm Gore-Tex shunt. Vascular access includes a 5 Fr venous sheath and a 3.3 Fr arterial sheath
Scenario 3	You are placing a bare metal stent in the left pulmonary artery of a 12 year-old (45 kg) patient with an extracardiac, non-fenestrated Fontan. The patient's only medication is aspirin 81 mg daily. Vascular access included a single 11 French venous sheath. Final diameter of the stent is similar to the right pulmonary artery. Hemodynamics at the conclusion of the intervention are satisfactory for Fontan circulation. The patient has no other comorbidities
Scenario 4	You are placing a bare metal stent in an adult with coarctation of the aorta. Vascular access includes a 12 French arterial sheath. The final stent diameter is 18 mm with a mild residual gradient (~5 mmHg). It does not cross or impinge on a brachiocephalic branch
Scenario 5	You are closing a large secundum atrial septal defect in an 8 year-old using a 22 mm AMPLATZER™ Septal Occluder device. Vascular access includes only a 9 French femoral venous sheath. The patient has severe right ventricular enlargement with normal systolic function; there is no history of thromboembolism or stroke

AV atrioventricular

Results

Demographics

Seventy-seven cardiologists completed the survey. The vast majority currently practice in the United States (81%), in an academic institution (88%). The median number of total procedures performed by the respondents per year was 200 (range 50–580); the median number of interventional procedures performed per year was 100 (range 30–300). Additional demographic and practice characteristics are shown in Table 2.

Pre-procedural Management of Anti-platelet Therapy

Respondents were first asked how they would generally manage patients who receive aspirin or clopidogrel prior to routine hemodynamic catheterization. While the majority of interventionalists ($n=60$, 78%) would continue aspirin prior to the procedure, only a third would continue clopidogrel ($n=26$, 34%). Nine respondents (12%) stated that they had too little experience with patients taking clopidogrel to describe their practice.

Scenario 1: Routine Hemodynamic Right and Left Heart Catheterization in Two-Ventricle Physiology

While the majority of responders (91%) anticoagulate at the beginning of routine right and left heart catheterization in this scenario, there was considerably less agreement regarding initial heparin dose. Most ($n=50$, 71%) favor an initial dose of 100 IU/kg, while fewer prefer 50 IU/kg ($n=14$, 20%) or 75 IU/kg ($n=3$, 4%). Three people (4%) recommended alternative dosing recommendations, ranging from 30 to 150 IU/kg (Fig. 1).

Scenario 2: "Pre-Glenn" Hemodynamic Right and Left Heart Catheterization

Respondents more uniformly heparinize at the beginning of a hemodynamic catheterization in a patient with single-ventricle heart disease, with only two respondents (3%) performing the procedure without anticoagulation. Similarly, the majority of operators ($n=58$, 77%) would administer 100 IU/kg of heparin, followed by 50 IU/kg ($n=10$, 13%), and 75 IU/kg ($n=4$, 5%). Three others preferred alternative dosing strategies ranging from 30 to 150 IU/kg.

Table 2 Respondent characteristics

Geographic location	
United States	62 (81%)
Canada	2 (3%)
Europe	9 (12%)
Other	4 (5%)
Clinical practice setting	
Public, academic	27 (35%)
Private, for-profit, academic	9 (12%)
Private, for-profit, non-academic	4 (5%)
Private, not-for profit, academic	32 (42%)
Private, not-for profit, non-academic	3 (4%)
Other	2 (3%)
Cath Lab location	
Pediatric lab within a freestanding children's hospital	45 (58%)
Pediatric lab within a non-freestanding children's hospital	16 (21%)
Combined adult and pediatric lab	14 (18%)
Lab within a non-hospital-based multi-specialty facility	1 (1%)
Other	1 (1%)
Total Cath Lab volume (per year)	
<100	2 (3%)
101–250	11 (14%)
251–400	30 (39%)
401–600	16 (21%)
>600	28 (36%)
Number of cardiologists performing Caths at Institution	
Median (range)	3 (1–6)
Respondents' own procedures performed (per year)	
All cases, median (range)	200 (50–580)
Interventional cases only, median (range)	100 (30–300)
Time since completion of fellowship	
<5 years	21 (27%)
5–10 years	21 (27%)
11–15 years	12 (16%)
16–20 years	8 (10%)
>20 years	15 (19%)
Completed senior interventional fellowship	
Yes	58 (75%)
No	19 (25%)

Scenario 3: Left Pulmonary Artery Stent Placement in Patient with Fontan

Seventy-three respondents (95%) acknowledged performing pulmonary artery stent implantation in a patient with Fontan-type circulation at least one time per year; the remaining four respondents did not answer questions for Scenario 3. There was general agreement among responders ($n=58$, 81%) to administer 100 IU/kg of heparin at the beginning of

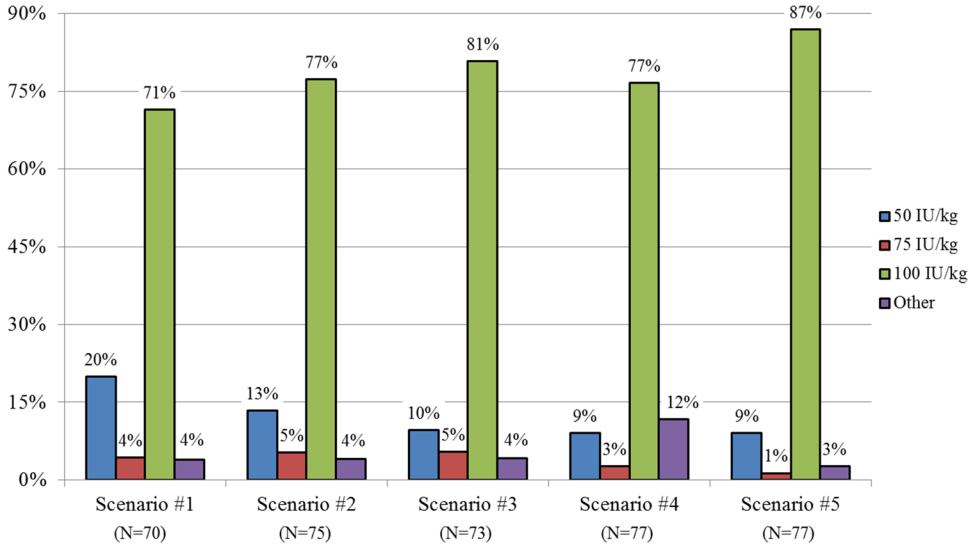

Fig. 1 Bar graph of the distribution of various initial heparin dosages for each scenario presented

the procedure. Seven respondents (10%) would administer 50 IU/kg and four (5%) would administer 75 IU/kg. Two respondents described non-weight-based dosages (3000 or 4000 IU), both less than 100 IU/kg based upon the patient weight provided in the case scenario (45 kg). Again, one respondent recommended an initial heparin dose of 150 IU/kg.

Scenario 4: Bare Metal Stent Placement in Patient with Coarctation of Aorta

All respondents endorsed performing stent placement for coarctation of the aorta at least one time per year and answered the questions relating to Scenario 4. Responses were similar to those for Scenario 3, with 77% ($n=59$) recommending an initial heparin dose of 100 IU/kg and 9% ($n=7$) favoring 50 IU/kg. Two respondents recommended 75 IU/kg, and one recommended 150 IU/kg. Eight others (10%) referenced a maximum total dose, ranging widely from 3000 to 10000 IU.

Scenario 5: AMPLATZER™ Septal Occluder Device Placement in Patient with Atrial Septal Defect

All respondents again endorsed performing ASD device closure at least one time per year. There was strong agreement for administering 100 IU/kg of heparin initially. As noted with previous interventional scenarios, a small minority ($n=7$, 9%) favored 50 IU/kg. The three remaining respondents recommended an initial dose of 70, 75, or 150 IU/kg at the beginning of the procedure.

Intraprocedural Monitoring and Reversal of Anticoagulation

When asked about timing of initial activated clotting time (ACT) after heparin administration, respondents' practice varied significantly by procedure type (Table 3). For Scenario 1, fewer than half of operators (46%) would measure ACT routinely during catheterization, while another 40% stated that their decision to measure ACT would depend upon the procedure duration. By contrast, a majority of

Table 3 Intraprocedural management of anticoagulation

	Scenario				
	1 ($n=70$) (%)	2 ($n=75$) (%)	3 ($n=73$) (%)	4 ($n=77$) (%)	5 ($n=77$) (%)
After administering heparin, would you check ACT levels during this procedure?					
Yes	46	63	89	92	84
No/would check only at conclusion of the procedure	14	7	5	3	13
Depends upon the duration of the procedure	40	31	5	5	3

ACT activated clotting time

respondents (63%) would measure ACT regardless of procedure duration for Scenario 2, either at regular intervals or prior to crossing the systemic-pulmonary shunt.

For interventional cases, the percentage of operators who would routinely measure ACT during the procedure ranged from 84% (Scenario 5) to 92% (Scenario 4). In all three cases, timing of ACT measurement varied. In all three scenarios, most of those who would monitor ACT would do so at regular, predetermined intervals (60–77%).

We next inquired about respondents' use of protamine for heparin reversal. For all scenarios presented, the majority of respondents (68–88%) would not routinely use protamine (Fig. 2). Protamine was most likely to be given after stent placement for coarctation of the aorta (32%) and least likely to be used after pre-Glenn hemodynamic catheterization (12%) or ASD device closure (13%).

Postprocedural Thromboprophylaxis

Respondents were asked about thromboprophylaxis preferences after Scenarios 2–5. Most of those surveyed (75%) would not empirically treat with anticoagulation (e.g., heparin) after the pre-Glenn catheterization of an infant with a systemic-pulmonary artery shunt. Of the remaining responders who would treat, 37% ($n=7$) commented that they would only administer anticoagulation if the shunt had been crossed with a catheter or wire.

Regarding thromboprophylaxis following pulmonary artery stent implantation in a patient with a Fontan (Scenario 3), there was strong agreement (97%) to use aspirin with general agreement (80%) that aspirin should be continued indefinitely. Of those who recommended aspirin, a significant minority (34%) preferred the addition of other antiplatelet/anticoagulant medications, ranging from short-term heparin treatment to lifelong warfarin. The two respondents who would not use aspirin both recommended lifelong warfarin alone.

Following coarctation stent placement (Scenario 4), most respondents (83%) recommended aspirin, the vast majority of whom (95%) recommend it alone. In most cases, respondents preferred aspirin thromboprophylaxis for 6 months (77%) with small minorities recommending aspirin indefinitely (14%), for 3 months (5%), for 12 months (3%), or for one month (2%).

Regarding thromboprophylaxis after ASD device closure, there was again strong agreement to prescribe aspirin (99%), with 97% of those respondents recommending 6 months of treatment. In lieu of aspirin, one respondent preferred clopidogrel for 1 month and warfarin for 6 months. Eight respondents who recommend aspirin (11%) preferred the addition of clopidogrel for anywhere between 1 and 12 months.

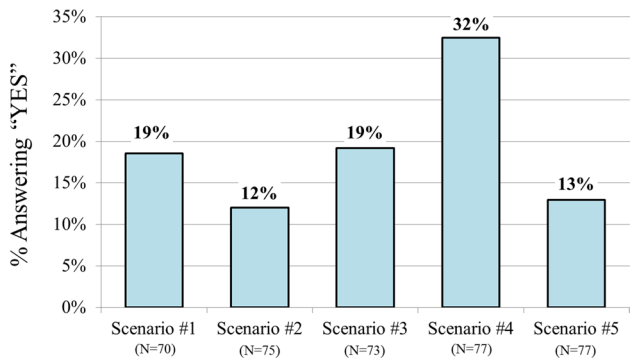

Fig. 2 Bar graph showing the percentage of respondents who answered "Yes" to the question, "Would you administer protamine for heparin reversal at the end of the study if ACT remains elevated?" for each scenario presented

Comparison of Responses to Demographic Variables

We next identified several questions that produced notable variability in responses and compared those responses to demographic characteristics (Table 4). To increase the power of this analysis, operators' responses and demographic characteristics were organized into binary variables. Responses were classified as yes/no or above/below an arbitrary threshold. Demographic characteristics used for this analysis included: geographic location (North America, non-North America); time in practice after fellowship (0–10 years, > 10 years); total number of interventionalists in practice (1–2, > 2); and operator case volume per year (< 200; ≥ 200).

Respondents practicing outside North America were less likely to administer 100 U/kg or more of heparin at the beginning of the two hemodynamic catheterizations presented (Scenario 1 and 2) than those practicing in North America. Respondents in larger practices were more likely to administer protamine for heparin reversal for Scenarios 1 and 5. Neither time in practice after fellowship nor operator case volume per year were found to be significantly associated with any of the selected responses.

Discussion

Our survey of 77 pediatric interventional cardiologists about their anticoagulation practice preferences revealed a notable degree of diversity of practice and deviation from published recommendations. As may be expected, the vast majority of respondents would routinely anticoagulate for diagnostic catheterizations (Scenarios 1, 2). However, the disagreement about initial heparin dosing for diagnostic and interventional procedures varied greatly. Published guidelines from the

Table 4 Comparison of selected responses with operator characteristics

	Geographic location			Years in practice			Interventionalists in practice			Operator cases per year		
	North America (%)	Other (%)	p	≤ 10 (%)	> 10 (%)	p	1–2 (%)	> 2 (%)	p	< 200 (%)	≥ 200 (%)	p
Stop aspirin prior to elective catheterization	20	31	0.47	24	20	0.79	22	22	1.00	16	21	0.77
Initial heparin dose ≥ 100 U/kg												
Scenario 1	81	38	*0.004*	70	77	0.60	80	68	0.29	62	80	0.11
Scenario 2	84	54	*0.026*	79	79	1.00	87	72	0.16	75	81	0..57
Scenario 3	85	64	0.10	86	77	0.37	87	79	0.54	81	83	0.77
Scenario 4	80	69	0.47	81	74	0.58	72	82	0.40	73	82	0.41
Scenario 5	88	92	1.00	88	89	1.00	81	93	0.15	85	91	0.49
Administer protamine at case end if ACT elevated												
Scenario 1	19	15	1.00	18	20	1.00	7	28	*0.032*	24	15	0.36
Scenario 2	11	15	0.65	10	15	0.50	3	18	0.07	16	9	0.48
Scenario 3	18	27	0.43	12	29	0.08	13	24	0.37	26	14	0.24
Scenario 4	34	23	0.53	29	37	0.47	31	33	1.00	39	27	0.33
Scenario 5	12	15	0.67	10	17	0.50	3	20	*0.040*	18	9	0.31

Statistically significant values ($p < 0.05$) are given in italics

ACT activated clotting time

American Heart Association (AHA) provided a Class I recommendation for an initial bolus of unfractionated heparin of 100 U/kg up to a maximum dose of 5000 U in children undergoing cardiac catheterization that includes arterial access, endovascular stent implantation, or device closure of an ASD [6]. The American College of Chest Physicians (ACCP) has recommended an initial dose of 100 U/kg for children undergoing cardiac catheterization that includes arterial access [7]. While heparin administration was advised prior to endovascular stent implantation, the ACCP did not provide dosage recommendations. Prior guidelines from the same group suggested a range of appropriate dosages (100–150 U/kg) rather than a single ideal dosage [8]. In our study, 19–29% of respondents to our survey deviated from the most recent AHA and/or ACCP guidelines. These findings are consistent with at least one single-institution report that showed only 50% complete adherence to the 2008 ACCP guidelines [9]. That study included all cases of antithrombotic therapy administered to pediatric inpatients over the study period and did not distinguish whether or how many instances involved cardiac catheterization. We also note that fewer non-North American than North American physicians administering ≥ 100 U/kg heparin for non-interventional cases. Because AHA and ACCP are primarily US organizations, this geographic variability in practice may be related to familiarity with those published guidelines.

We noted a broad range of practice related to monitoring of anticoagulation during catheterization. For diagnostic Scenarios 1 and 2, a large number of respondents would determine the timing of initial ACT level based upon the duration of the procedure or would not measure ACT until case conclusion. A larger proportion of respondents favored monitoring ACT levels at regular, preset intervals for interventional cases (Scenarios 3–5). Of note, AHA guidelines recommend initial ACT measurement be performed 1 h after heparin loading bolus and every 30 min, thereafter [6]. While the questions posed in our survey were not designed to specifically define the degree to which operators comply with this recommendation, their responses suggest a variety of approaches to procedural monitoring of ACT.

One area in our study where respondents showed very high agreement with AHA guidelines was regarding thromboprophylaxis after stent implantation in a patient with a Fontan (Scenario 3). As written, the guidelines are sufficiently broad to allow for compliance without uniformity of practice. Specifically, the AHA provides a Class I recommendation for low-dose aspirin for at least 6 months after any non-coronary artery endovascular stent implantation and a Class IIa recommendation for the use of warfarin or low molecular weight heparin with or without anti-platelet for 3–6 months followed by aspirin after stent implantation in "high-risk" situations, such as a non-pulsatile circuit (e.g., Fontan) [6]. With this in mind, we considered the use of either aspirin and/or warfarin for a total of 6 months after Fontan stent implantation to comply in principle with these recommendations. Despite the diversity of specific

post-procedural thromboprophylaxis practices reported in our survey, only one response did not comply with either of these recommendations. In contrast, 19% of operators would not comply with either of the above recommendations after coarctation stent implantation (Scenario 4), including 14% who would not recommend antiplatelet or anticoagulant therapy at all.

Nearly all respondents complied with AHA recommendations for low-dose aspirin prophylaxis after ASD device closure [6]. Only one respondent endorsed an alternative treatment strategy of clopidogrel for 1 month and warfarin for 6 months. This high degree of practice uniformity may be due to the presence of both device-specific, manufacturer-established treatment recommendations and published expert guidelines, which consistently advise at least 6 months of antiplatelet therapy [10].

Although we did not ask specifically about operators' awareness or understanding of published guidelines relative to the discussion above, or about their rationale for deviating from these guidelines, our survey results underscore that expert guidelines may not necessarily reflect real-life practice, and when strong evidence for practice recommendations is lacking, a deeper understanding of generally accepted practices may be beneficial when formulating standardized guidelines. In many instances, data upon which these recommendations are based are sparse or non-existent. In such situations, guidelines are necessarily derived from upon expert consensus or research performed in adults. It is highly likely that clinical practices that stray from rigid guidelines may produce similarly acceptable clinical results. To this point, at least one study demonstrated no difference between a 50 and 100 U/kg loading dose of heparin [11].

One practice for which there are no published guidelines is the use of protamine for heparin reversal. We did not ask respondents why they do not administer protamine routinely. Protamine use varied between scenarios, and for two scenarios correlated significantly with higher operator volume. This finding may reflect operators' comfort level with managing protamine-related complications. Protamine has been reported to cause a hypotension due to decreased systemic vascular resistance [12], which may partly explain the reluctance of the majority of our survey respondents to use protamine on a regular basis. Other factors that may influence practice, such as the availability of anesthesia support during catheterization, were not assessed in our survey. A systematic review of protamine reactions reported a low rate of anaphylactic reactions to protamine of 0.2–0.7% [13]. Protamine use has been extensively studied in the vascular surgical literature. Despite earlier concerns for an increased risk of thrombosis with the administration of protamine after carotid endarterectomy, the preponderance of data suggest that protamine does not increase this risk and decreases the risk of post-operative bleeding [14, 15]. The risk of vessel thrombosis is a common concern after cardiac catheterization, particularly in neonates and small infants [16]. However, protamine has never been shown to be a risk factor for vessel thrombosis. Also considering the known frequency of access site bleeding complications after cardiac catheterization [3–5], the potential benefit of routine protamine use may outweigh the risks. Ultimately, a more systematic analysis of the risks and benefits of protamine in the congenital cardiac catheterization lab would provide opportunities for improving the quality of care provided therein.

Limitations

We acknowledge that the nature of our survey-based study limits our ability to drawn definitive or nuanced conclusions regarding the real-life practice of pediatric and congenital interventional cardiologists. We rely on the accuracy of survey respondents' answers to our questions and are unable to audit survey results for reliability. While we discussed the pooled responses in the context of relevant published practice guidelines, the survey was not designed to systematically analyze these differences. In addition, by allowing responses from any operator who performs the described procedures only once per year, we may conflate the opinions of those with very different levels of experience. We also recognize the natural evolution of clinical practice and make no claim that our results reflect current or future practice patterns.

Conclusions

Management of anticoagulation in the congenital cardiac catheterization lab varies from operator to operator and may deviate from formal published recommendations. The clinical implications of this inconsistency in practice are unclear. Our study may provide some initial insight and context for discussion regarding anticoagulation in a field of increasingly heterogeneous interventional techniques and patient substrates. Future studies, including randomized-controlled trials, would be helpful to better define "best practices" for peri-procedural thromboprophylaxis in patients with congenital heart disease.

Author Contributions NWT contributed to the concept and design of this study; data collection, analysis and interpretation; drafting and critical revision of the article; statistical analysis; and final approval of the manuscript. BHG, BMG, and GJM contributed to the concept and design of this study; data analysis and interpretation; critical revision of the article; and final approval of the manuscript.

Compliance with Ethical Standards

Conflict of interest The authors have no financial or other conflicts of interest related to this study.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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