Increased risk of cardiovascular perforation during ECMO with a bicaval, wire-reinforced cannula

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1. Background

Cardiac or major vascular perforation is a rare but known complication associated with intravascular access, hemodialysis and extracorporeal membrane oxygenation (ECMO) [1,2]. Perforation from vascular access and hemodialysis can occur in the superior vena cava (SVC), but has also been reported in the right atrium (RA) during cannulation are sporadic and have included injury to the SVC, perforation might focus on vascular access and hemodialysis can occur in the superior RA and right ventricle[2,8,9].

Anecdotal or institutional responses to cardiac or major vascular perforation and its morbid consequences may discourage reporting. With brief reports and series exist, the sporadic and infrequent nature of cannula perforation was much higher for the wire-reinforced bicaval design 3.6% (10/279) as compared to catheters designed for the atrial position, 0.1% (1/1203, p-value = 0.29) at 7 different ELSO centers with 23 ELSO centers responding (17% response rate). The incidence of perforation was much higher for the wire-reinforced bicaval design 3.6% (10/279) as compared to catheters designed for the atrial position, 0.1% (1/1203, p-value < 0.0001). Review of the FDA’s MAUDE database revealed 19 adverse events related to the bicaval cannula design, 16 of which were hemorrhagic pericardial effusions or tamponade.

Conclusion: These findings suggest a relatively high rate of cardiac perforation associated with the dual lumen bicaval cannula. This may be related to inherent differences in cannula design or the IVC positioning required by the design.

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Purpose: Cardiac or major vascular perforation is a rare but serious risk of ECMO. We sought to determine if perforation rates are related to cannula design.

Methods: We utilized three methods to evaluate perforation on ECMO. 1. The ELSO registry was queried to establish the historical rate of hemorrhagic pericardial tamponade. 2. ELSO centers were surveyed regarding cannula related perforation events and brands of cannulas used over a four year time period (January 2008–March 2012). 3. The FDA’s MAUDE database was reviewed looking for adverse events related to ECMO cannulas.

Results: The historical rate of hemorrhagic pericardial tamponade in the ELSO registry was 0.53% (~1985–2010, ELSO registry). In the survey there were eleven reports of cannula-related perforation, 0.74% (11/1482 p-value = 0.29) at 7 different ELSO centers with 23 ELSO centers responding (17% response rate). The incidence of perforation was much higher for the wire-reinforced bicaval design 3.6% (10/279) as compared to catheters designed for the atrial position, 0.1% (1/1203, p-value < 0.0001). Review of the FDA’s MAUDE database revealed 19 adverse events related to the bicaval cannula design, 16 of which were hemorrhagic pericardial effusions or tamponade.

Conclusion: These findings suggest a relatively high rate of cardiac perforation associated with the dual lumen bicaval cannula. This may be related to inherent differences in cannula design or the IVC positioning required by the design.

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Though it is difficult to distinguish the impact of specific design variables in individual patients, the FDA device monitoring database provides a surrogate means of tracking design variations. Because of the small volumes associated with ECMO, differing brands have design characteristics that change infrequently and the design characteristics tend to be unique to each brand. Thus tracking adverse events between cannula brands may highlight design flaws (e.g. wire reinforcement or catheter length) that predispose to perforation.

Herein we seek to better describe the etiology and epidemiology of ECMO access perforation. We also seek to determine if perforation rates are related to cannula design and/or intended catheter position.

2. Methods

We utilized three methods to evaluate cardiovascular perforation on ECMO. This was done under the direction of Hawaii Pacific Health IRB study number HPHRI 2012-127.

The Extracorporeal Life Support Organization (ELSO ECMO Registry of the Extracorporeal Life Support Organization (ELSO), Ann Arbor, Michigan) registry was queried to establish the historical rate of cannula perforation on ECMO. The ELSO registry maintains a voluntary database comprised of all known cases in which ECLS is performed at an ELSO center. The ELSO database provides general case details, complications associated with ECMO, in addition to overall patient outcomes. The ELSO database was queried for “Cardiovascular: tamponade: blood” as an indicator for cardiac perforation on ECMO. While not perfect, hemorrhagic pericardial tamponade provided the closest clinical surrogate for cardiac/vascular perforation within the ELSO registry. The registry was used as a historical comparison point to contrast with the survey; this was done because registry data did not completely overlap temporally due to the retrospective nature of the ELSO database.

We then surveyed ELSO centers about types of ECMO cannulas used, specific perforation events, and radiographic techniques used for placement over a four year time period (Jan '08–Mar '12). We limited the survey to this timeframe because it roughly encompassed the market availability of a new cannula design: a high flow, dual-lumen bicaval cannula. Survey invites were sent via email with follow up email/contact to encourage participation. Respondents were able to respond in either MS word format or a SurveyMonkey internet response. The survey was designed as a simple overview and inquired about the total number of ECMO cases, the number involving cannula perforation, whether or not the perforation resulted in death, brands of cannulas used at the center, estimated frequency of use of each brand, and the brand of cannula involved in perforation events. Results of the survey were compiled in an MS Excel spreadsheet. Cannula perforation rates were calculated for each cannula type and statistical significance was determined using the Fisher exact test.

Lastly we queried the FDA’s Manufacturer and User Device Experience (MAUDE) database. We limited the timeframe of the database review from 2008 to 2012, trying to approximate the same period as the survey. MAUDE was reviewed looking for adverse events related to different types and brands of ECMO cannulas. The database was queried for events related to “ECMO” and “ECMO cannula” under the category of “Catheter, Cannula and Tubing, Vascular, Cardiopulmonary Bypass” devices. Reports of ECMO cannula related events within the MAUDE database were then reviewed independently by two reviewers to ensure reported events were pertinent to the study.

3. Results

The historical rate of hemorrhagic pericardial tamponade for respiratory neonatal ECMO in the ELSO registry was 0.53% (1985–2010). The reported rate of hemorrhagic pericardial tamponade on cardiac ECMO is historically higher at 1.8%.

The email/internet survey response rate from ELSO centers was 17%, with twenty-three ELSO centers responding (23/133 centers surveyed). There were eleven reports of cannula-related perforation for a rate of 0.74% (11/1482; p-value = 0.29 when compared with the ELSO registry) with perforations observed at 7 different ELSO centers. Overall, 23 ELSO centers responded for a 17% response rate. During the time period of our review there were approximately 12,533 ECLS cases reported to ELSO. Of these approximately 67% were placed on ECLS for respiratory indications (the sub-group we studied), 26.5% for cardiac indications, and the remainder for ECPR. Thus, from the ELSO registry it can be estimated that there were approximately 8397 patients on ECLS for respiratory indications (the population of our survey). Of these patients, our survey captured an estimated 17.6% of the total ELSO population over the survey time-period (1482/8397).

When rates of perforation were distinguished by brand/design, the incidence of perforation was much higher for the wire-reinforced bicaval design 3.6% (10/279). In contrast, we observed a perforation rate of 0.1% (1/1203), p-value < 0.0001 in catheters that were designed to be positioned in the atrium. When cardiac perforation did occur, it generally happened in the right atrium (10/11 or 91%); all survey atrial perforations were associated with a wire-reinforced design and all but one involved the bicaval design. One-half (5/10) of the atrial perforations resulted in death, all five with the bicaval design. There was also one perforation in the IVC with the bicaval catheter.

Review of the FDA’s MAUDE database revealed 19 adverse events related to the bicaval ECMO cannula, sixteen of these involved hemorrhagic pericardial effusions or tamponade. Twelve of these were surgically confirmed perforations; ten were atrial in location, one was in the SVC and one site of perforation was not reported. With the bicaval cannula, there were four cases of tamponade in which a perforation was not confirmed. One patient underwent sternotomy for tamponade, but a perforation was not found, two were managed with drains only, and in one patient with confirmed tamponade the patient expired prior to intervention. There were also two reports of cracked cannulas and one of a torn vein with cannula removal.

There were 40 other events reported for other brands of ECMO cannulas, most of which were relatively mundane such as cracking or kinking of cannulas or leakage around one brand of femoral cannula. There was one report of SVC perforation with an atrial cannula. There were also several reports of clotting of a pediatric VA arterial cannula and multiple reports of kinking, dislodgement, cracks, air aspiration and slipped connections between various brands. As the MAUDE database reporting is device variable, not all reports to the database included surgical findings.

4. Discussion

While a review of the ELSO database provides a historical rate of hemorrhagic pericardial tamponade, these survey results and the MAUDE database review both suggest that variations in cannula design may have safety implications that go beyond the functional characteristics of the design. Though the overall rate of perforation noted in the survey is similar to historical perforation rates, when cannulas are separated out by brand there is a relatively high rate of cardiac perforation with the bicaval cannula design. If brand distinctions are indicative of design variables such as wire reinforcement or catheter length, it appears that either the bicaval catheter design or bicaval positioning of a catheter has a high rate of cardiac perforation.

That said, it is difficult to distinguish which specific design nuances of the bicaval cannula might predispose to perforation [14]. The bicaval cannula differs from other dual lumen ECMO cannulas in a few ways: overall length, space between ports, wire reinforcement (some), and its intended bicaval position [15]. One recent review concluded that cardiac perforations observed with an ECMO cannula
was due to the "wire reinforced nature of the cannula design" [10]. We would argue from the evidence gathered in this study that, while it appears to be currently impossible to fully determine the contribution of each design variable (wire vs bicaval position), the bicaval position seems to contribute more risk of perforation as compared to wire reinforcement alone. In other words, many atrial ECMO cannulas are wire reinforced, yet we did not see perforation rates that approximate those observed with the bicaval design.

In order to position the catheter according to the design specifications, the bicaval design often requires placement with wire and/or ECHO guidance in addition to standard chest radiographs [16,17]. In our experience, we have noted excellent flow through the bicaval cannula even when the cannula becomes dislodged or malpositioned, thus flow characteristics may not be indicative of malposition [18]. In neonates we have experienced malpositioning of the dual lumen cannula and adopted a policy of frequent ECHO cardiography [19]. We have found that correct placement in the bicaval position is initially fairly easy, but that the catheter can slip out of the IVC with minor changes in patient position and can rest against the RA without noticeable changes in flow dynamics. In some cases we have been successful at bedside repositioning, but in others we have found the longer length of the cannula to be difficult to manage when it becomes dislodged from the cava because of the proximity of the SVC intake ports. We currently place the bicaval cannula 1–2 cm deeper into the IVC than we did on early patients as it seems to provide more stability to the placement of this device. Whether this simple modification of placement will prevent cases of perforation requires further study.

While our review did not distinguish rates of perforation between neonatal, pediatric or adult populations, the visible trends in our review infer that perforation was much more common with the smaller (13 Fr) bicaval cannula. Others have reported right ventricular perforation in an adult patient with the bicaval cannula design [20], but overwhelmingly the reports in our review and the MAUDE database are associated with neonatal perforation and the 13 bicaval cannula. However, the bicaval design can be advantageous in certain situations because the design does seem to allow for improved flow characteristics. These characteristics may be very useful and safe in larger patients or with ECHO surveillance of the position of the bicaval cannula [21]. Further study of the design could prove to be beneficial.

Surgeons should be aware of potential limitations in the oversight within sub-categories of medical device manufacturing/approval. Most surgical and interventional devices are approved by the FDA in a manner that is much less rigorous than that used in the drug approval process. Moreover, because there are many broad categories within "already approved medical devices," many new devices with genuinely innovative differences are brought to market quickly and placed under the umbrella of predicate devices. In some cases, this is beneficial as innovative ideas are rapidly introduced for the benefit of patients [22,23]. In other cases, some innovations may have unforeseen and unstudied repercussions that go unnoticed because design implications are not prospectively predictable [24,25].

This study is limited by multiple factors. Though the survey response rate is consistent with the expected response for an external survey, the nature of the survey might predispose centers with a history of perforation to disproportionally respond. Against this, in this study the overall perforation rate observed did not differ significantly from the ELSO historical rate, making this unlikely. Another possible problem is that the proxy "hemorrhagic pericardial tamponade" under-appreciates other cannula related complications that might stem from non-cardiac perforation (e.g. hemothorax) and thus underestimate injury from other cannula designs. Thus this study tends to highlight cardiac complications as opposed to noting other cannula related complications that can also have devastating consequences [26–30]. Another weakness is the overall incidence of cannula perforation on ECMO (<1%) makes statistical analysis difficult because small changes in reported numbers can greatly affect statistical differences related to perforation rates. Because individual centers may experience rare or few perforation events, centers may consider events as isolated whereas a larger review may demonstrate a systemic problem. This underscores the necessity of participation in national databases such as ELSO. Lastly, the MAUDE database is subject to many limitations such as selection error or bias. Entry is voluntary and the reports often filter through the device manufacturer which may bias the report. We attempted to limit selection errors and other biases by conducting independent reviews and cross-checks of the database.

With these limitations in mind, these findings suggest a relatively high rate of cardiac perforation associated with the bicaval cannula design. We conclude that this is likely secondary to the specific IVC positioning required by the design. Pediatric surgeons should be aware that minor differences in device design may represent functional differences in kind, and that minor changes in cannula design may impact clinical care in unpredictable ways. Because of the sub-specialized nature of our field, pediatric surgeons need to be proactive in evaluating design nuances whenever possible as new devices are introduced.

References

Dr. Charles Stolar:

Discussant: Charles Stolar (Santa Barbara, CA):

Response: Dr. Gwendolyn Garnett:

Discussant: David Sigalet (Calgary, AB):


The whine is just something and then there was one ventricular perforation in an adult patient. The perforation site was mostly the SVC. That was very rare though, the right atrium. We did not have any in the IVC. The other experience. The baby survived but it was an awkward moment. These are hazardous cannulas. That thing that David mentioned — what’s quite big and it’s stiff and it has a point on the end of it. The question is how many of these perforations occurred after the cannula was placed? In other words, you alluded to it — some were days later. I would be very interested to know how many were a problem with the initial placement and then how many occurred when people moved or the baby moved afterwards. Can you tell us?

Response: Dr. Gwendolyn Garnett: The vast majority of them occurred several days after the cannulation, and very few at initial insertion. Just in our institutional experience we found that correct positioning on insertion isn’t terribly difficult but later on the catheter has the tendency to migrate out of the IVC and rest against the right atrium and then there is where the perforations occur.

Discussant: Charles Stolar (Santa Barbara, CA): I just have a comment and a whine. I really appreciated you bringing this to our attention. The comment is that I was involved in one of these perforations. It happened right in front of my eyes. It was a newborn we were putting on ECMO and fortunately doing it with echocardiography control and I could see the cannula go right through the floor of the right atrium. The reason that happens is because as you come down the IVC what is straight ahead of you from this sharp pointed thing that David mentioned — what’s straight ahead is the floor of the right atrium, not the IVC. Even with ultrasound guidance and even with a wire you can still perforate the floor of the right atrium. These are hazardous cannulas. That’s just my own personal experience. The baby survived but it was an awkward moment. We call that troublesome bleeding.

Response: Dr. Gwendolyn Garnett: Most of the perforations do occur in the right atrium. We did not have any in the IVC. The other perforation site was mostly the SVC. That was very rare though, and then there was one ventricular perforation in an adult patient.

Dr. Charles Stolar: But the target is the floor of the right atrium like I said. The whine is just something — we all deal with devices in children.

You can no longer get the SciMed oxygenator for ECMO. You have to use the hollow-fiber Quadrox oxygenator that have their own problems, and why don’t we have the SciMed oxygenators anymore? Because they don’t make them. They become an orphan device. This is just yet another example that anybody that uses devices in children they are extrapolated from the adult world and we are left with what device people make for us. I don’t pretend to have a solution to the problem but I’m certainly willing to whine about this. I think we all deal with this and this is a device developed for the adult world that we have extrapolated to the pediatric world and it unmasks problems. Thank you for bringing this to our attention. I hope you will scale this to other issues we have with devices that are used in children.

Discussant: Dr. Ronald Hirschl (Ann Arbor, MI): So one of the problems with this cannula is that in order to hold the cannula in the IVC you have to have enough length and in a newborn that difference between being in the IVC and out is very small. I just want to make that comment. Trying to keep this cannula in the IVC is a problem which may be why we are seeing late perforation, but we’ve also seen very early perforations, that is, at the time of cannulation. One of the questions I have is whether fluoroscopy was used and, as Charlie mentioned, an Echo may not be good enough to be able to put the wire into the IVC and get the cannula safely in the IVC. In fact, what we’ve seen is that the wire will go down into the right atrium, curl, and then go back down into the IVC. That’s a very dangerous situation. As a result, we no longer will put this cannula in at the University of Michigan without fluoroscopy, period. That’s true of all ages. The problem is that we have had enough perforations during cannulation that we think it’s dangerous to just use echo. Anyway, my question is if you know how many were done percutaneously versus open and also whether fluoroscopy was used?

Response: Dr. Gwendolyn Garnett: For the second point, it looks like most centers use echo to do it but there are reports of using fluoroscopy also to place the cannula. As far as the first point is concerned, I do not have exact numbers if they were open or percutaneous but I think the majority were open because most of the cannula perforations have occurred with the #13 French cannula, so the very small one on the neonates where you’d usually take an open approach and very few with any of the cannulas of larger size.

Dr. Ronald Hirschl: Just as an additional comment, Origins is about to come out with a wire round cannula that will be in the size of our needs and hopefully that does not need to be in the IVC and it will allow us, as the pediatric surgery community, to have a cannula that doesn’t need to be in the IVC but is wire round and doesn’t kink and bend and so on.

Discussant: Dr. Oluyinka Olutoye (Houston, TX): I very much enjoyed your presentation and of course the comments of my esteemed senior colleagues that have gone forth ahead. I stand to give a slightly different opinion from what has been said. I think this is definitely a major concern with perforation, and obviously a child with a perforation is a major problem. I think what you haven’t reported in what you’ve said, even though very experienced pediatric surgeons have noticed this complication, is a lot of these catheters are being placed by cardiologists and non-surgeons because everybody seems to think this is an easy catheter to place, and so there is that element of it as well. I think it is interesting that you have noted that most of the complications are seen in the #13 French cannula group which is actually a smaller catheter as opposed to a #31 French huge catheters that we place in teenagers at times. I think the point is very important because in terms of — this is a new device. We
can't place it like we've placed all the other old devices. We really need to be very familiar with how it is being placed. I very much agree that echocardiogram is not always sufficient at times, because many times on echo you can't see the guide wire going through and using fluoroscopy to help is important. I think it is clear from what you've said that most of these do not necessarily occur at the time of insertion if you are doing it very carefully. A lot of them occur afterwards which is a factor of where it is positioned. Many times people think it is in good position and it is not. With a right ventricular perforation, what was the catheter doing in the right ventricle? It had no reason being there in the first place. Again, I think this is a new technology. Before it is widely adopted, people have to be very careful and not just infer that we can do it the way we have always done it. Specific benefits are there for a bicaval catheter but I think it is also important to realize that with every new device we can't just jump on the bandwagon without taking adequate precautions. I congratulate you for bringing this to our attention.