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INFORMED CONSENT:

Mechanical thrombectomy for intermediate risk pulmonary embolism

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ABSTRACT An informed consent article using a set of publications to develop an informed consent conversation for a patient with an acute pulmonary embolism being considered for pulmonary artery thrombolysis.

Keywords: *pulmonary embolism, mechanical thrombectomy, informed consent*

Clinical-Social Context

Shawn Turner [pseudonym] is a 33-year-old man who was at work at a loading dock when he had a sharp pain in the right side of his chest associated with shortness of breath. He was worried the symptoms meant he was having a heart attack, so he informed his boss, who understood the seriousness of the situation and took him directly to the emergency room of the local hospital. Mr. Turner had a history of factor V Leiden mutation and multiple deep vein thrombi in the past, so a CT—Pulmonary Embolism protocol angiogram in the Emergency Department was ordered. That study revealed an acute pulmonary embolism in the right distal main and segmental branches along with a possible pulmonary infarct and mild right ventricular strain.

At that point, the patient felt disappointed that he had a clot in his lungs as he previously only had experienced them in his legs. About three weeks prior to this admission for pulmonary embolism, he came to the emergency room and was evaluated for deep vein thrombosis where it was determined that the rivaroxaban that he had been taking for years was no longer working because of another DVT in the right popliteal vein was found. At that time, the hematologist recommended he transition to apixiban. The rationale for this decision was not recorded in the medical record. Mr. Turner asked the hematologist if he could finish the last two weeks of the rivaroxaban before transitioning to the apixiban. The hematologist agreed. Again, the rationale for this decision was not recorded in the medical record. Four days prior to recent symptom onset he started taking apixiban at a therapeutic dose.

At the time of admission, the admitting physician and the in-house resident physician reviewed the decision of possible pulmonary artery thrombolysis using EkoSonic Pulmonary Embolism (EKOS) system, prompted by the finding of “mild right heart strain” and the relative distal location of the thrombus. In the Emergency Department, Mr. Turner’s blood pressure was 140/72, respiration 16, pulse 88, pulse oximetry on room air was 95%-98%, and

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temperature 98.3 degrees Fahrenheit. Because the patient's clinical status was reassuring, the treating physicians decided the risks of harm from the thrombolysis procedure outweighed the potential benefits. This was based on the presumption that the procedure would involve ultrasound guided thrombolytics and included the risks of catheter induced trauma and thrombolytic induced bleeding. Because the clinical decision had high level of consequences, the in-house physician reviewed recommendations for thrombolysis, and the case was re-evaluated with the guidance of the algorithm for treating Pulmonary Emboli published in Up-to-Date. Again, because of the stable clinical status of the patient, the same conclusion and clinical decision was reached—continue heparinization without thrombolysis.

During the second conversation, the treating physicians discussed the issue of “remaining clot burden” in the lower extremities, to determine the risk of subsequent potential pulmonary emboli, which would increase the risk of lung damage. Doppler ultrasound of the lower extremities was ordered. Because the patient was clinically stable, the attending physician on the night of admission thought the most important clinical question was, “Is intervention necessary to prevent Chronic Thromboembolic Pulmonary Hypertension (CTEPH)?” Given the subsequent large thrombotic load remaining in the legs and in future years of life, this was the rationale for asking if the patient would benefit from an IVC filter with anticoagulation.

Unknown to the above treating physicians, the Emergency Department (ED) physician had reached the same conclusion regarding thrombectomy based on “*Calculated RV/LV ratio is 0.95. There is no evidence of contrast reflux into the inferior vena cava.*” The ED physician documented:

*Work-up shows PE, at this time patient will be continued on IV heparin and be admitted for further evaluation and treatment, no significant signs of heart strain on CAT scan and ratio less than 1, at this time patient stable for admission to floor, plan discussed family medicine team.*¹

Mr. Turner's pain was well controlled with hydromorphone and he was started on a heparin drip. The patient was informed that the risks of the thrombolysis outweighed the benefits based on the clinical management decisions described above.

A doppler ultrasound of the lower extremity was ordered given his leg swelling and it revealed an occlusive thrombus involving the right popliteal and posterior tibial veins as well as an occlusive thrombus involving the left popliteal and entire superficial femoral vein and posterior tibial vein. Upon finding large bilateral clots in both lower extremities, vascular surgery was consulted to consider inferior vena cava filter in addition to anticoagulation. The rationale for asking about an IVC filter together with anticoagulation was the subsequent large thrombotic load remaining in the legs and in future years of life. This patient had failed anticoagulation therapy alone and was at risk for repeated pulmonary emboli.

When Mr. Turner was informed that he might need an IVC filter and that he should be NPO, he felt slightly confused but was agreeable to the plan. “I just want to get better and feel safe.”

Later the vascular surgeon came to the hospital and talked to him. The vascular surgeon felt like he was a candidate for thrombectomy and wanted interventional radiology to evaluate him for the procedure. The patient indicated that the vascular surgeon informed him that heparin alone “might not do the job, that the clot might be there for months, and that he might not feel better with heparin alone.”

Interventional radiology evaluated him and informed Mr. Turner that he ‘really should get a mechanical thrombectomy as the clot is straining the right side of his heart’. He told the interventional radiologist that he had watched a lot of videos about how thrombectomies are done and he is very fascinated by them. He thought it's a very “cool procedure” and that he would like to try it out, especially since he was told by the physician's assistant from interventional radiology that it's a very safe procedure. When interviewed after the procedure, Mr. Turner recalled he was told that the procedure had almost no complications and it would help immensely.



The informed consent documented in the chart was a generic “dot phrase” auto-generated by the Electronic Health Record (EPIC) that had no details included, not even identifying to whom the informed consent was discussed or any potential harms of the procedure.

Before the patient consented to the procedure, an explanation was provided to the patient (and/or representative) by me of the anticipated benefits, the likelihood of success, and potential risks, side effects, and complications of the procedure(s). The patient (and/or representative) acknowledged understanding what is expected and what may happen after the procedure when recovering. The patient (and/or representative) was also informed of the significant alternatives and their associated risks, benefits and side effects, and the probable consequences of not having the procedure(s) performed. No guarantees, promises, or assurances have been made to the patient (and/or representative) about the results that may be obtained or the consequences that may follow the procedure(s).¹

Clinical Question

What is an appropriate basis for making clinical decisions to provide mechanical thrombectomy for intermediate risk pulmonary embolism?

Description of Related Literature

A PubMed search: ("thrombect*" AND "mechanic*" AND "Pulmonary embol*" {Filtered by Clinical Trial}) yielded eight results. Only one study was for pulmonary embolus without thrombolysis.² Reviewing the MeSH and repeating the search: ("Pulmonary Embolism"[MeSH]) AND "Thrombectomy"[MeSH] filtered by clinical trial yielded 10 results with no other related trials.

In PubMed, when the FLARE registry by Tu, et. al. was screened for related studies (Cited by), another case series and literature review were identified.³

Review of references for the Mathbout article identified a case report.⁴

Review of in Google Scholar of “Related Articles” revealed the PERFECT trial which was the only relevant article out of only 13 studies.⁵ The paucity of clinical research was explained by the fact that most trials used thrombolytic medications instead of mechanical embolectomy alone or studied only “massive pulmonary embolism”—neither of which was true in the Clinical-Social Context. The Registry by Tu, et. al. specifically included intermediate risk patients, which was important to the care of this patient.

Using Google search, “Inari FlowRetriever” showed the website of the manufacturer.⁶ Listed on that web Page were other registries.

The FLAME, PEERLESS trial and the CLOUT trial are registries that are still recruiting patients. The FLASH Registry has preliminary results presented at a conference. The outcomes were disease oriented, but full publication was not available.⁷

A new search was done by deleting the “Clinical Trials” filter in PubMed (“FLASH Registry AND pulmonary embolism”), which identified two articles describing the FLASH registry.^{7,8}

Critical Appraisals

FLASH is a report of a registry intended to assess safety and efficacy of the FlowTrieve system. Patients registered were those over 18 years old with intermediate or high-risk acute PE. This is an interim analysis of the first two-hundred and fifty patients, who were recruited at the investigator’s discretion. Outcomes included major adverse events (including device-related death, major bleeding and device- or procedure-related adverse events) within 48 hours of procedural intervention. In this interim analysis, they found 1.2% composite major adverse events within 48 hours, and 0.4% all-cause mortality within 30 days.

There is high risk of conflict of interest amongst investigators, including investigators receiving money from the device manufacturer. This leads to a high risk of selection bias. There is no information on how many patients at each institution had pulmonary embolism,



and which patients with pulmonary embolism were not chosen to have this intervention. The patients investigated in this registry trial may not represent the entire population of patients with pulmonary embolism.

The mMRC (Modified Medical Research Council) Dyspnoea Scale was used in this study.⁹ This scale might not be appropriate for acutely hospitalized patients with dyspnea because this is a scale used to determine baselines for patients with chronic respiratory disease.

The FLASH registry is a SORT level 3 evidence, because it is essentially a large case series.⁷

The FLARE study is prospective, single-arm, multi-center registry. It registered hemodynamically stable patients 18 to 75 years old with symptoms of acute proximal PE confirmed on CT. The intervention was FlowTriever mechanical embolectomy to remove the embolus from the pulmonary arteries. There was no comparison group. The outcome measured was the change in RV/LV ratio, which is a disease specific measure of undetermined significance. The size effect in the outcome measure was modest, but statistically significant with before-after measures. There were also major adverse events in 3.8% of patients.

Similar to the FLASH registry, there are many weaknesses to this evidence. One major weakness is no comparison group. There are no long-term outcomes reported, because the study end-point was 30 days. The outcomes are not patient-oriented. There are also high risks for conflicts of interests because the study design and data collection process included input from the study sponsor, Inari Medical. Many of the investigators received funds from various companies, including Inari Medical. The manuscript was written by a medical writer funded by Inari Medical.

This is a SORT level 3 evidence, due to a lack of patient-oriented outcome.¹⁰ It is also a case series.

There were several small case series or case reports found that did not add additional information.

The Grade of Recommendation is C—expert opinion based on flawed case series.¹⁰ Deciding what to say, what not to say, how to phrase the conversation, and the emotional overtones of the conversation are all clinical decisions and therefore are representative of Clinical Decision Science. The relevant Translational Social Science falls in the category of discourse analysis (not discussed here.) The following conversation is provided for role modelling as learning.

Informed Consent

Flesch Reading Ease = 83.2; Flesch-Kincaid Grade Level 4.4

"You had blood clots in your legs. Blood flows from your legs into your lungs. The clot started in your legs, but it flowed downstream into your lungs. Now you have a blood clot in your lungs. Small clots in the lung are not a worry. Very big clots can cause death. We think the clot you have is medium sized.

"A big lung blood clot can stop blood flow through the lungs and back into your heart. A big blood clot can make it harder for your heart to pump blood past the clot.

"There are different ways to treat a blood clot. Your body can break down the clot the way a scab on your knee heals. Blood thinners prevent more clots from forming. You have been taking blood thinners, so you are familiar with that treatment. It's important to remember that blood thinners make it harder to stop bleeding. The bleeding could happen anywhere, including your brain, so it's important to be careful and not fall.

"You are not very sick right now. So, you have options about what to do. It would be okay to let your body heal this clot—the important part is to prevent another clot getting into your lungs.

"Another way to treat this is by giving medicine directly over the blood clot. The medicine dissolves the clot quickly. A local numbing medicine is used before inserting a plastic tube into a vein. You may also be given some medicine to help you relax and feel more comfortable. The plastic tube is guided to the blood vessels in your lung where the blood clot is. When it gets to the blood clot, the medicine to break down the clot is given.



"The blood clot can also be taken out; this is called a thrombectomy. One of the doctors that spoke with you recommended using a device called FlowTrieve. This is like using a wire to unclog a pipe in your house. Sort of like a plumbing problem. The best studies available looking at the FlowTrieve are preliminary. Other treatments have been studied more. Risk of bad outcomes with the FlowTrieve is about to 1-4%.

"Generally the procedure is safe. But doctors have to tell you all of the things that might possibly go wrong. The risks are the blood clot goes somewhere else and damage an important organ. It can scratch parts of your lungs or your heart. It can cause an abnormal heart rhythm. It can poke a hole in a blood vessel. It can cause bleeding. It can cause an infection because it breaks the skin. The blood clot can come back. You might still have pain when breathing after. With sedative medication, there is a risk of decreased breathing or breathing fluid or food into the lungs.

"You will still need a blood thinner after the procedure.

"People with a big blood clot should have it removed. People who are not as sick can choose what to do. Your blood clot is less severe and your heart is working well. The reason you might want to do it is a commonsense argument—get rid of the clot because it doesn't belong there.

"The most important thing is to prevent another one of these episodes"

Clinical Application

Based on this clinical-social context, we explored the resources available in the hospital setting of our clinical practice. Many physicians were unaware that mechanical embolectomy was available for patients; other doctors continue to report the prior standard of care, the EkoSonic Pulmonary Embolism (EKOS) system, as what they would expect. This is an opportunity for the physician practice group to discuss and explore appropriate management in the current context.

New Knowledge Related to Clinical Decision Science

This case demonstrated how we build an evidence base for new technologies. It is difficult to compare these initial lower quality studies to highly studied, established therapies. Although this was presented as a case of therapy, when does research become accepted practice?

It is important to let the patient know if the procedure they are getting needs further evaluation. This case is an example of the need for transparency between physicians and patients. Transparency is one of the ethical foundations of professionalism.¹¹ There are other published examples that the physician's opinion determines what information and what recommendations are given to patients.¹²

Shared decision-making is an important step. For this to happen, the patient must have an understanding of the disease, intervention and outcomes. This is not always available in clinical practice. The "dot-phrase" documentation means that there was no ability to reconstruct the actual events, and the patient's perception was that the decision making was "confusing". The statement that there was "practically no harm" is contradicted by the single study which documented Major Adverse events.

The original question of preventing CTEPH asked when the vascular surgeon was consulted was never addressed. Why did each physician have such varying perspectives on the major clinical management questions and decisions for this patient?

Clinical judgment can be distorted when clinicians have an emotional and financial investment to a potential therapy. Oftentimes they believe that this therapy has great benefit to patients and their enthusiasm for treatment exceeds the available evidence.¹³ However, evidence-based care needs to balance these considerations.

A relevant research question within the domain of Clinical Decision Science is to compare the consent rate of patients with intermediate risk pulmonary embolism using the above consent versus the consent used for the registry trials.



Conflict of Interest Statement

The authors have no conflict of interest to declare.

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