Forensic Considerations in a Series of 14 Deaths of Patients with a Left Ventricular Assist Device

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ABSTRACT

Introduction: To better understand the forensic implications of death with a left ventricular assist device (LVAD), we reviewed all deaths that were reported to a regional medical examiner jurisdiction involving patients who had an LVAD.

Methods: Medical examiner case files between January 2012 and September 2018 were searched for “LVAD” and “left ventricular assist device” to identify deaths that were reported to the medical examiner involving a decedent who had an LVAD at the time of death.

Results: During the study period, a total of 14 deaths were reported to the regional medical examiner involving decedents who had an implanted LVAD at the time of death. The average age at death was 64 years, with a range from 40 to 81 years. The underlying cardiac disease leading to LVAD implantation was ischemic heart disease ($n = 9$), nonischemic dilated cardiomyopathy ($n = 4$), and chemotherapy-related cardiotoxicity ($n = 1$). Of these 14 deaths, 2 deaths were due to loss of power to the LVAD, 1 death was due to traumatic subdural hemorrhage occurring in the setting of anticoagulation therapy required by LVAD implantation, and 1 death was due to femur fracture following a fall.

Discussion: Medical examiners should be familiar with the potential complications of LVADs, especially those complications that may prompt consideration of non-natural manners of death. Medical examiners should also be aware of the tools and investigative strategies that may assist in the investigation of LVAD-related deaths. *Acad Forensic Pathol.* 2019 9(3-4): 200-211

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INTRODUCTION

A left ventricular assist device (LVAD) is an implantable medical device intended to provide systemic circulatory support to a failing heart (1,2). Implantation of an LVAD in a patient with severe systolic heart failure can dramatically improve quality of life (3) and provide a longer window of time for either recovery of heart function or heart transplantation (4). Initially, LVADs were implanted as a temporary life-sustaining device until a donor heart becomes available (bridge-to-transplant), but more recently, LVADs have increasingly been implanted as a permanent device without intent to proceed to heart transplantation (destination therapy) (5,6). This expansion in LVAD usage as destination therapy has significantly increased the number of LVADs implanted (5,7-12) and increases the likelihood that a patient who has an LVAD implanted will die with the LVAD in place. These two factors increase the likelihood that medical examiners will encounter an LVAD in the course of a death investigation. Therefore, medical examiners should be familiar with the usage and operation of LVADs and their potential complications. At a minimum, medical examiners/coroners (ME/Cs) should be familiar with the complications that may raise concern for a non-natural manner of death. In particular, medical examiners ME/Cs should be aware that patients with LVADs require a continuous and consistent power supply to ensure that adequate systemic circulation is maintained. Systemic power outages, battery failure, accidental disconnection, or other events that may interrupt the power supply could result in sudden unexpected death where a non-natural manner of death could be considered.

In this study, we retrospectively reviewed deaths reported to a regional medical examiner involving patients who had an implanted LVAD at the time of death. The regional medical examiner jurisdiction includes a major academic heart transplant center. We reviewed the circumstances surrounding death, whether jurisdiction was assumed by the medical examiner, whether an autopsy was performed, and the final certification of the underlying cause and manner of death.

METHODS

Medicolegal death investigation records (MDILog, Occupational Research and Assessment) for a regional medical examiner system in the United States that includes a major academic medical center were searched for “LVAD” and “left ventricular assist device” to identify deaths that had been reported to the medical examiner between January 2012 and September 2018. Records were reviewed to ensure that the decedent had an implanted LVAD at the time of death. Temporary, short-term systemic circulatory support devices such as catheter-based pump devices (e.g., Impella device) and intra-aortic balloon pump devices were excluded. For each case, the medical examiner case file was examined, including autopsy report, death certificate, and scene investigation report. Jurisdiction by the medical examiner was considered to be assumed if the death certificate was signed by the medical examiner. Data were tabulated in a Microsoft Excel worksheet. This study was evaluated via an institutional automated “IRB Research Wizard” application and deemed to be exempt from institutional review board review.

RESULTS

During the 6-year study period, a total of 14 deaths of patients with implanted LVADs were reported to the regional medical examiner system. The average age was 64 years, with a range from 40 to 81 years. There were nine male patients and five female patients. The average time between LVAD implantation and death was 37 months, with a range of zero to 88 months.

Of the 14 reported deaths, a scene investigation was performed in three cases, autopsy was performed in three cases, and the medical examiner signed the death certificate in eight cases. Based on review of the death investigation file, the reason for reporting the death to the medical examiner was possible traumatic death ($n = 5$), possible therapeutic procedure-related death ($n = 3$), loss of power to LVAD unit ($n = 2$), unknown/jurisdiction declined ($n = 2$), sudden death at home ($n = 1$), and previous history of alcohol abuse ($n = 1$). All LVADs were placed as destination therapy.

The underlying natural disease resulting in cardiac failure was ischemic heart disease ($n = 9$), nonischemic dilated cardiomyopathy ($n = 4$), and acute myeloid leukemia chemotherapy-related cardiotoxicity ($n = 1$). The manner of death was natural in 12 cases and accident in two cases. The two accidental deaths resulted from trauma—one due to traumatic subdural hematoma and one due to femoral fracture. Among the deaths that were certified as natural for manner of death were two deaths involving unintentional loss of power to the LVAD. In both cases, accidental manner of death was considered, but ultimately natural manner of death was chosen. In both of these cases (discussed in more detail below), an autopsy was performed. The third autopsy was performed in order to document a traumatic subdural hematoma due to a fall in the setting of anticoagulation therapy for the LVAD. Case data for each death reported to the medical examiner are reported in **Table 1**.

Detailed History For Case #1

The decedent was a 62-year-old man with a history of end-stage systolic heart failure due to ischemic heart disease and implantable cardioverter-defibrillator (ICD) placement, who underwent a Heartmate II LVAD implantation as destination therapy approximately 2 years prior to death. At the time of LVAD implantation, he also underwent two-vessel coronary artery bypass and tricuspid valve annuloplasty. His postimplantation course was complicated by multiple episodes of driveline infection and *Staphylococcus aureus* bacteremia, requiring hospitalization. Following each hospitalization, he recovered and reported feeling well and was able to maintain an active lifestyle.

One evening, he was attending a concert at a casino that was located one hour from his home, when his low battery alarm started to go off and he realized that he had forgotten to bring his backup batteries. He immediately alerted casino staff and a 911 call was

Table 1: Deaths Reported to the Regional Medical Examiner Involving Patients with Left Ventricular Assist Devices

Case	Age	Sex	Autopsy	Immediate COD	Underlying COD	Manner
1	62	M	Y	Loss of battery power	Ischemic heart disease	Natural
2	72	M	N	Unknown	Ischemic heart disease	Natural
3	69	M	N	Sepsis	Chemotherapy-related cardiomyopathy for acute myeloid leukemia.	Natural
4	64	F	N	Cerebral hemorrhage	Non-ischemic dilated cardiomyopathy	Natural
5	62	F	N	Multi-organ failure	Ischemic heart disease	Natural
6	72	M	Y	Failure to connect power supply	Ischemic heart disease	Natural
7	59	F	N	Gastrointestinal hemorrhage	Ischemic heart disease	Natural
8	40	M	N	Sepsis	Non-ischemic dilated cardiomyopathy	Natural
9	59	M	N	Thromboembolic stroke	Non-ischemic dilated cardiomyopathy	Natural
10	63	M	N	Cerebral hemorrhage	Ischemic heart disease	Natural
11	67	F	N	Complications of femoral fracture	Ischemic heart disease / blunt trauma	Accident
12	81	M	N	Unknown	Ischemic heart disease	Natural
13	57	F	Y	Traumatic subdural hematoma	Ischemic heart disease / blunt trauma	Accident
14	69	M	N	Gastrointestinal hemorrhage	Non-ischemic dilated cardiomyopathy	Natural

placed. When emergency medical services (EMS) arrived, he was placed in an ambulance to be transported to a regional medical center but he went into cardiac arrest while en route. His ICD delivered three shocks, without return of normal rhythm. Cardiopulmonary resuscitation and advanced cardiac life support efforts were attempted, but not successful, and he was pronounced dead in the emergency room.

The death was reported to the regional medical examiner and jurisdiction was accepted. A death scene investigator responded to the local hospital emergency room and obtained the LVAD controller and batteries for possible further interrogation. An autopsy was ordered.

At autopsy, the presence of severe ischemic heart disease with two-vessel coronary bypass was confirmed. The heart was markedly enlarged (1070 g). The LVAD was found to have intact inflow and outflow anastomoses and the device was removed from the heart. The LVAD pump, LVAD controller device, and batteries were returned to the manufacturer for additional examination. The ICD was also removed and returned to the device manufacturer for interrogation. Examination of the LVAD device and LVAD controller at the manufacturer revealed no device-related issues. Small depositions of blood but no large thrombus was identified within the rotor unit. Interrogation of the LVAD controller log file indicated that the LVAD had been operated normally for approximately 10 continuous hours before there was a Low Battery Advisory arm. Nine minutes later, the alarm progressed to a Low Battery Hazard alarm. The hazardous low voltage condition continued for approximately another nine minutes until there was a complete cessation of power. Examination of the two batteries indicated that both batteries were fully depleted.

Based on the circumstances and device interrogation, it was determined that depletion of battery power to the LVAD device was the immediate cause of death. The underlying cause of death was atherosclerotic and hypertensive cardiovascular disease. Significant contributory causes of death included obesity, tobacco use, and LVAD, and ICD placement. The manner of death was certified as natural.

Detailed History for Case #7

The decedent was a 72-year-old man with a history of end-stage systolic heart failure due to ischemic heart disease, status post two-vessel coronary artery bypass graft surgery, left circumflex coronary artery stent placement, and placement of an ICD. Approximately five years prior to death, he underwent implantation of a Heartmate II LVAD as destination therapy. His clinical course following LVAD implantation was complicated by gastrointestinal hemorrhage likely due to acquired von Willebrand disease and anticoagulation therapy, multiple driveline infections, pump thrombosis, and chronic anemia likely due to hemolysis. Approximately one year before his death, he was found to have ascending colon cancer and underwent right hemicolectomy without significant complications. More recently, he developed an inguinal hernia and was undergoing evaluation for surgical repair.

He was staying in a local hotel with his wife while attending follow-up appointments at the heart transplant center. Early one morning, the decedent's wife was awakened by the sounds of the decedent walking around the hotel room. They spoke briefly and he said that he had had a tough night. He then collapsed to a kneeling position on the floor with his head on the bed. She realized that he was not plugged into the wall unit which is his usual power source while sleeping. He was too far from the wall unit for her to plug the controller back into the power source. She called the front desk of the hotel for help and EMS arrived shortly after. The first responders reported that upon arrival to the room, an audible alarm was going off. The first responders initially attempted resuscitation and then realized that he had a do-not-resuscitate order in place, so resuscitation efforts were discontinued and he was pronounced dead at the scene. The medical examiner was notified of the death and a scene investigator responded.

At the scene, the investigator noted an elderly individual lying between two hotel beds with nearby evidence of resuscitation efforts. An LVAD controller device and two portable battery packs were present on one of the beds. The decedent's driveline was disconnected

from the controller device, and the controller device was disconnected from both battery packs. Interview of the first responders revealed that they attempted to reconnect the decedent to the controller device and the portable batteries during the attempted resuscitation and then disconnected all cables upon discontinuation of the resuscitation (possibly in an attempt to stop the alarm sound). The initial configuration of the controller device to the batteries was unclear. The decedent was transported to the medical examiner office for an autopsy. The LVAD controller device and batteries were also transported with the body.

Autopsy confirmed the presence of ischemic heart disease and the typical postsurgical changes seen with LVAD placement such as myocardial fibrosis in the region of the left ventricular apex where the inflow conduit is attached and epicardial fibrosis in regions where the outflow conduit is in contact with the heart. The LVAD inflow conduit anastomosis with the left ventricle was intact and patent, as was the LVAD outflow conduit to the ascending aorta. There was moderate to marked endocardial fibrosis of the left ventricular cavity. There was no gross evidence of device-related infection such as driveline infection or pump device pocket infection. Importantly, there was no evidence of pulmonary emboli or device-related thrombosis. The brain showed remote infarctions of the left parietal and right occipital lobe consistent with previous thromboembolic strokes.

Interrogation of the LVAD controller device at the transplant center revealed that both fully charged portable batteries had been connected to the controller device early in the morning likely while the decedent's wife was still sleeping. Around the time that the decedent had been seen walking around the hotel room by his wife, both batteries were disconnected from the controller device. Disconnecting both batteries would have triggered an audible alarm, which was likely the alarm that was heard by the first responders. The driveline was disconnected from the controller around the time that the EMS first responders were in the room.

The cause of death was certified as ischemic cardiomyopathy (status post LVAD placement) due to atherosclerotic coronary artery disease. The manner of death was certified as natural.

DISCUSSION

Numerous studies have examined short- and long-term adverse events including death in LVAD patients (13-16), but to our knowledge, this is the first study to examine the deaths of LVAD patients occurring in a forensic setting. As more patients are implanted with LVADs as destination therapy, LVAD patient deaths are more likely to come to the attention of medical examiners, and a subset will require a complete death investigation including autopsy. In this study, of the 14 deaths of patients with LVADs that were reported to the medical examiner, two were associated with loss of power to the LVAD unit and two were associated with external trauma. These cases highlight the complexity that may be associated with the forensic death investigation of LVAD-related deaths and the issues that may arise with cause and manner of death determination, particularly in those deaths where loss of power is suspected. For these reasons, medical examiners should be familiar with the components of LVADs, standard methods of examination of the native heart and LVAD at the time of autopsy, complications that may be associated with LVAD therapy, resources that may assist in the investigation of an LVAD-related death, and standardized strategies for certifying cause and manner of death. A brief table of recommended best practices for the forensic investigation of LVAD-related deaths is presented in **Table 2**.

Components of an LVAD

The components of an LVAD device generally consist of 1) inflow conduit, 2) pump device, 3) outflow conduit, 4) driveline, 5) controller, and 6) battery packs. These components are shown in **Images 1 and 2**. The inflow conduit, pump, and outflow conduit are located entirely within the body, the driveline connects the pump within the body to the controller outside the body, and the battery packs are connected to the controller and worn on a vest external to the body. In-

Table 2: Recommended Best Practices for the Forensic Investigation of Left Ventricular Assist Device (LVAD) Related Deaths

1	Obtain detailed medical history including specific brand of LVAD, date of implantation, institution where implantation occurred, prior complications, and underlying natural disease
2	Obtain detailed account of circumstances surrounding death, including configuration of LVAD components when found, power source at time of death and charge status of batteries
3	Have low threshold for accepting jurisdiction if there is concern for loss of power to LVAD unit, or if there is concern for trauma as an underlying cause or contributory cause of death (anti-coagulation therapy is required for LVAD devices).
4	If jurisdiction is accepted, obtain the LVAD controller unit and battery packs for interrogation either by the manufacturer or by the clinical provider.
5	If other cardiac devices are present, such as an ICD or pacemaker, consider interrogation of those devices for additional information.
6	Consider consultation with a cardiovascular pathologist for the evaluation of the heart and LVAD device.
7	Consider non-natural manners of death including accident, suicide, homicide, or undetermined, based on the overall results of the death investigation.

Image 1: Detached and disassembled continuous flow left ventricular assist device (Heartmate II) components consisting of inflow conduit (A), pump device (B), driveline (C), outflow conduit (D) and ascending aorta anastomosis (E). Note that the inflow and outflow conduits can be unscrewed from the pump device to allow easier inspection of the conduits and pumps for thrombosis.

Image 2: Heartmate II controller device (arrow head) from case #7 found on hotel bed with partially detached portable battery packs (arrows).

ternally, the inflow conduit is attached to the left ventricular apex and delivers blood from the left ventricle to the pump device, which then drives blood through the outflow conduit to the ascending aorta. By convention, the inflow and outflow conduits are named relative to the pump, not the patient. In addition to the inflow and outflow conduits, the pump is attached to a driveline which is a cable that provides power and instructions to the LVAD through the external controller and battery packs. The driveline exits the skin, usually in the upper abdominal region, and is a common site of infection. Externally, the driveline is attached to a controller unit which provides instructions to pump, monitors the pump function, and provides alerts and other warnings. The controller unit is generally powered by two portable battery packs. During sleep, while the batteries are recharging, the controller device may be powered directly by a wall unit which is plugged into an electrical outlet.

Examination of the LVAD and Heart

When examining the internal components of an LVAD at autopsy, the device should first be separated from the heart and aorta. This usually involves incising the myocardium of the left ventricle surrounding the attachment site of the inflow conduit. The outflow conduit usually consists of synthetic conduit material that may be incised near the attachment point to the ascending aorta. The subsequent evaluation should then follow recommendations provided by the Society for Cardiovascular Pathology for the evaluation of LVADs in surgical pathology (17). Briefly, both the inflow and outflow conduits should be examined for thrombosis, vegetations, kinks, obstructions, or defects. In some devices, the inflow and outflow conduits may be unscrewed from the pump device, allowing easier examination of the conduits and the pump. Examination of the internal structure of the pump will require sending the device to the manufacturer, but some pump components may be viewable through the conduit attachment sites. The pump device typically consists of either a rotor device or centrifugal impeller. Photographic documentation of the LVAD components is recommended.

Examination of a heart with an LVAD should be directed toward identifying the underlying natural disease as well as any anatomic findings associated with the LVAD device. Dense myocardial and epicardial fibrosis is typically present in the region of the left ventricular apex where the LVAD inflow conduit is inserted into the left ventricle. Focal thrombus may be identified in the apex of the left ventricle or surrounding the inlet conduit with some devices (18). Evidence of acute and/or chronic thromboembolic phenomena may be present in other organs. The aortic valve leaflets may have been sutured closed to prevent aortic regurgitation from the LVAD outflow conduit into the ascending aorta. Alternatively, the aortic valve leaflets may have naturally developed commissural fusion due to constantly being in a closed state during periods of high LVAD flow relative to native left ventricular systolic function, which operates in parallel to the LVAD circuit (19).

Complications of LVAD Therapy

For the purposes of death investigation of LVAD-related deaths, it may be useful to divide the complications associated with LVAD devices into two categories: 1) medical complications, and 2) external complications.

The most common medical complications seen with LVAD therapy are infections, bleeding, thrombosis, and strokes. In a study of deaths in patients with LVADs as destination therapy, the most common mechanisms of death were multi-organ failure, hemorrhagic stroke, and progressive heart failure (15). The increased risk of bleeding is multifactorial, including anticoagulation therapy necessary to prevent device thrombosis and acquired von Willebrand factor deficiency, due to shear stress-induced proteolysis of von Willebrand factor molecules as they are carried across the LVAD surfaces (20,21). Despite these hemorrhagic risks, thrombosis remains a significant complication and systemic thromboembolism leading to stroke is also a major complication of LVAD therapy.

Deaths that result from medical complications of LVAD therapy are unlikely to be reported to the medical examiner, but medical examiners should still be

familiar with them because the specific mechanism of death may not be apparent at the time the death is reported. This is especially true when deaths occur suddenly and unexpectedly outside of a health care setting. In such cases, additional investigation, including autopsy, may be necessary to establish the specific mechanism of death. An LVAD-related death should not be automatically declined for jurisdiction simply because a significant natural disease is present.

Deaths that result from external complications such as loss of power, or external trauma, are more likely to be reported to the medical examiner. Deaths in LVAD patients due to complications of external trauma such as a fall should be handled in the same manner as other traumatic deaths and are largely straightforward. In many instances, anticoagulation therapy for the LVAD should be included as a contributory cause of death. However, deaths due to suspected power loss to the LVAD will likely require a more detailed death investigation by the medical examiner.

Loss of power may result from depletion of batteries, accidental or intentional disconnection from a power source, systemic power outages, device malfunction, or battery failure. The need for the patient to be constantly connected to a power supply requires careful planning for routine daily activities. For example, each evening, patients must remember to disconnect the LVAD controller from the portable batteries and connect to the wall power charger and also remember to recharge the batteries overnight. In the morning, the patient must check to ensure that the batteries have been fully charged and then disengage from the wall power unit and reconnect to the portable batteries. Anytime LVAD patients embark upon prolonged outings, they must remember to bring backup batteries, and they should have a plan to find an alternative power supply if needed. Failure to follow these detailed procedures can result in catastrophic consequences.

The scene investigation of an LVAD-related death where loss of power is suspected is largely directed toward identifying the circumstances that led to the loss of power. In addition to a detailed history from witnesses, family members, and health care providers,

regarding the circumstances surrounding death, interrogation of the LVAD controller may provide important information concerning the timing and sequence of events surrounding the interruption of the power supply. In both of these reported cases, the ability to interrogate the LVAD controller was helpful for the death investigation. However, it is important to note that despite interrogation of the LVAD controller and the ICD, the circumstances surrounding the interruption of power supply to the LVAD still remained somewhat unclear and speculative in one case. As with all deaths, the certification of cause and manner of death must rely upon all available sources of information, and conversely, the significance of any single piece of information must be interpreted in the context of the overall case.

Cause and Manner of Death Certification

The underlying cause of death in LVAD-related deaths can usually be attributed to the underlying cause of end-stage systolic heart failure. However, it is also important for statistical and public health purposes to document the particular mechanism or complication that preceded death. For example, thromboembolic disease, pump failure due to thrombosis, driveline infection, or battery failure are all distinct complications of LVAD therapy that could be identified through a detailed death investigation and may have regulatory implications. Because of the increasing use of LVADs as destination therapy, LVAD-related deaths are more likely to occur at home or in other non-health care settings. Therefore, forensic autopsy-based data on LVAD complications will likely play a more critical role in the continuing evaluation of the safety and efficacy of LVADs.

The manner of death in both cases involving loss of battery power was certified as natural, though accident was seriously considered in both cases. In case #7, undetermined was also considered for manner of death due to uncertainty surrounding the circumstances of the disconnection from power. For both cases, the most appropriate classification may have been therapeutic complication since the death resulted from a known complication of LVAD therapy (22).

However, therapeutic complication is not an option for manner of death in this medical examiner jurisdiction and it is the practice of the certifying medical examiner to certify the manner of death as natural, if therapeutic complication would have otherwise been more appropriate. Accident would have been appropriate, for example, if disconnection from the power source had resulted from a trip and fall. While natural, accident, and therapeutic complication are likely to be the most common manners of death in LVAD-related deaths, it is also important to consider the possibility of suicide. Although quality of life for LVAD patients is generally improved, LVAD implantation may be associated with anxiety and depression in some patients (23,24). Suicide due to deliberate disconnection from a power source, or disconnection of the driveline, may be difficult to ascertain without prior expression of intent but should at least be explored with family and caregivers. Of note, LVADs are frequently deactivated as a palliative end-of-life procedure due to the underlying natural disease (15), and in such situations, the most appropriate manner of death is natural. The circumstances are analogous to the cessation of other life-sustaining medical devices such as ventilators at the end of life. Finally, to our knowledge, homicide due to deliberate disconnection of an LVAD has not been previously reported but is certainly a possibility that should be considered. Because LVAD patients are largely reliant upon their caregivers, concerns for neglect or abuse may also arise and raise the possibility of homicide as a manner of death. A thorough scene investigation along with systematic autopsy examination would be essential in such scenarios.

CONCLUSION

In conclusion, ME/Cs and death investigation personnel are likely to encounter LVAD-related deaths with increasing frequency as more devices come to market and the shortage of available donor transplant hearts persists (3,4). Most deaths that occur in patients with an LVAD may not require a full autopsy, due to the presence of extensive natural disease and associated known therapeutic complications. However, being aware of complications that need more attention is central to discovering both causes and manners

of death that may be unexpected and could have industry-related and population-based impacts, such as mechanical device failures. Parsing through all of the potential mechanisms of death to accurately develop a set of differential diagnoses is paramount to highlighting the correct manner of death, which may be initially shrouded in the complexities of natural disease.

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