Intracranial Hemorrhage in Patients with Durable Mechanical Circulatory Support Devices: Institutional Review and Proposed Treatment Algorithm

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■ BACKGROUND: **Spontaneous intracranial hemorrhage (ICH) is frequently managed in neurosurgery. Patients with durable mechanical circulatory support devices, including total artificial heart (TAH) and left ventricular assist device (LVAD), are often encountered in the setting of ICH. Although durable mechanical circulatory support devices have improved survival and quality of life for patients with advanced heart failure, ICH is one of the most feared complications following LVAD and TAH implantation. Owing to anticoagulation and clinically relevant acquired coagulopathies, ICH should be treated promptly by neurosurgeons and cardiac critical care providers. We provide an analysis of ICH in patients with mechanical circulatory support and propose a treatment algorithm.**

■ METHODS: **We retrospectively reviewed medical records from 2013–2016 for patients with a durable mechanical circulatory device at Banner–University of Arizona Medical Center Tucson. All patients with suspected ICH underwent computed tomography scan of the brain. Anticoagulation was managed by the cardiothoracic surgeon.**

■ RESULTS: **In 58 patients, an LVAD ($n = 49$), TAH ($n = 10$), or both ($n = 1$) were implanted. Both acquired von Willebrand disease and spontaneous ICH were diagnosed in 5 patients (8.6%) who underwent LVAD implantation. Seven neurosurgical procedures were performed in 2 patients. The overall mortality rate was 60%. Two patients had little or no deficits after treatment with modified Rankin Scale score of 1 and 2, respectively.**

■ CONCLUSIONS: **We propose a novel treatment algorithm to manage patients with a LVAD or TAH and ICH, implemented in a multidisciplinary manner to best avoid neurologic and cardiovascular complications.**

INTRODUCTION

Spontaneous intracranial hemorrhage (ICH) in patients with coagulopathies is a frequently encountered neurosurgical diagnosis at most tertiary care centers. Management of such patients requires basic knowledge of the coagulation cascade, frequent collaboration with providers from both pharmacy and critical care for appropriate reversal of coagulopathies, and swift clinical judgments to determine if and when it is safe to surgically intervene. Patients with durable mechanical circulatory support devices, including left ventricular assist devices (LVADs) such as the HeartMate II (Thoratec Corporation, Pleasanton, California, USA) and HeartWare (HeartWare, Framingham, Massachusetts, USA), and biventricular assist devices such as the total artificial heart (TAH), comprise a relatively new population of coagulopathic patients who are increasingly encountered by neurosurgeons.

LVADs are implanted artificial hearts that have been used over the last several decades by cardiologists and cardiovascular surgeons to manage advanced systolic heart failure. The device is

Key words
- Coagulopathy
- Intracranial hemorrhage
- Intraparenchymal hemorrhage

Abbreviations and Acronyms
AvWD: Acquired von Willebrand disease
CT: Computed tomography
EVD: External ventricular drain
FFP: Fresh frozen plasma
ICH: Intracranial hemorrhage
INR: International normalized ratio
IPH: Intraparenchymal hemorrhage
LVAD: Left ventricular assist device
PCC: Prothrombin complex concentrate
SDH: Subdural hematoma
TAH: Total artificial heart
vWF: von Willebrand factor

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connected to the left ventricular apex and artificially pumps nonpulsatile blood through to the ascending aorta, bypassing the failing left ventricle (Figure 1). Initially, these devices were used as a bridge to heart transplant to aid circulation, but with advancement in durable technology and a decrease in available donors, in recent years, LVADs are being increasingly considered as a destination therapeutic option to transplant.[1] TAHs are implanted in a smaller subpopulation of patients and are generally reserved for patients with severe biventricular heart failure who cannot be treated with LVAD implantation or patients with anatomic considerations that preclude LVAD implantation.[2] The left and right ventricles and valves of the native heart are excised and replaced by the TAH, which is connected to the great vessels, completely replacing the ventricular system to artificially pump blood to the lungs and systemically. Together, LVADs and TAHs have effectively provided bridging therapy to heart transplantation as well as destination therapy as permanent implants.

Although durable mechanical circulatory support devices have improved both survival and quality of life in the large population of patients with advanced heart failure, they are associated with complications.[3] Hemorrhage (both perioperative and delayed), right heart failure, hemolysis, thromboembolism, and device failure are known complications associated with implantation.[1] The potential for thrombosis within the pump itself and thromboembolism possibly leading to stroke are the main reasons why most of these patients require treatment with warfarin. Therefore, the risk of spontaneous hemorrhage, particularly ICH, both early after device implantation and later is significant. Management of ICH in the setting of supratherapeutic warfarin therapy is not a novel clinical scenario for neurosurgeons, as the reversal of warfarin is routinely performed with fresh frozen plasma (FFP) or prothrombin complex concentrate (PCC). However, there is further reason for hemorrhage in some patients with LVADs resulting in severe cases of ICH, making both reversal of coagulopathy and treatment of hemorrhage in these patients more difficult than expected.

The overall risk of any major hemorrhage, which most often occurs within 30 days of LVAD implantation, is approximately 50%.[4,5] Approximately 25% of patients require surgery for a hemorrhagic event. In several large studies examining outcome in patients with LVADs, ICH was diagnosed in 3%–11% of the patients.[4-6] Warfarin and antiplatelet therapies contribute to the risk of device-related thrombus formation and stroke, increases the risk of hemorrhage. However, it is believed that patients with LVADs acquire an inherent coagulopathy that is not necessarily due to anticoagulation, as their risk of hemorrhage is greater than can be expected from anticoagulation alone.[7] Acquired von Willebrand disease (AvWD) is a rare disease that was previously associated only with lymphoproliferative disorders and aortic stenosis. It is now thought to significantly contribute to the overall risk of hemorrhage in patients with LVADs.[8]

von Willebrand factor (vWF) is expressed by endothelial cells and facilitates platelet aggregation at sites of vascular injury. Furthermore, it functions as a carrier of factor VIII in the plasma and prevents its proteolytic degradation, thereby enhancing circulating levels of factor VIII and increasing its delivery to sites of vascular injury.[9,10] It is believed that high shear stress within nonpulsatile flow LVADs and narrow pulse pressure produce a conformational change in the molecule and a resultant decrease in vWF multimers that circulate in the plasma. This phenomenon occurs in most patients after LVAD implantation and contributes to gastrointestinal tract bleeding in some patients, but it is yet to be specifically analyzed in patients with ICH.[8,11,12] Some mechanical circulatory devices, such as the TAH and some types of LVADs, function via pulsatile flow, thus mimicking more physiologic blood flow, and have been shown to be associated with lower shear stress, but these devices have not been associated with a decreased incidence of AvWD or hemorrhagic complications.[13]

At our institution, which is a large academic medical center with a high clinical volume of both heart transplant surgery and neurosurgery, ICH is one of the most feared complications following LVAD and TAH implantation. Because of necessary anticoagulation and clinically relevant acquired coagulopathies, ICH in this patient population is severe and should be treated promptly and comanaged by both neurosurgeons and the cardiac critical care team. In this article, we analyze, for the first time to our knowledge, ICH encountered in patients with mechanical circulatory support devices and propose a treatment algorithm.

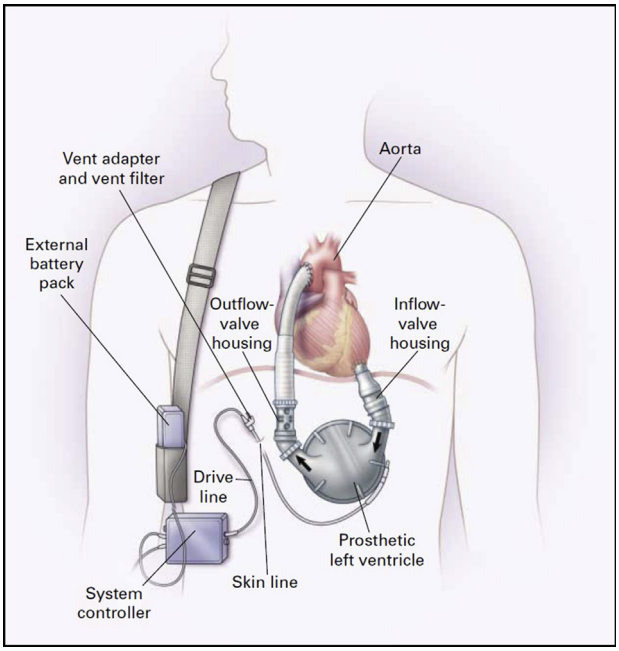

Figure 1. Left ventricular assist device. The afferent component is inserted into the left ventricle, where blood flows into the prosthetic left ventricle. Blood is pumped out of the device through the outflow cannula and into the ascending aorta, where it then circulates systemically. A percutaneous line carries an electrical cable from 2 batteries (only the right is shown) that power the prosthetic ventricle and electronic controls. (Reprinted with permission from Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, et al. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med.* 2001;345:1435-1443.[3])

MATERIALS AND METHODS

Between 2013 and 2016, 58 patients with a durable mechanical circulatory device were managed at Banner—University of Arizona Medical Center Tucson. Medical records, results of neurologic examinations, laboratory values, and radiographic images were retrospectively reviewed after approval by the Institutional Review Board (1605607496). Patients diagnosed with ICH after implantation of an LVAD were analyzed. The modified Rankin Scale was used to assess neurologic function both before and after diagnosis of ICH.

All patients with suspected ICH were evaluated with a computed tomography (CT) scan of the brain. The neurosurgical team was consulted after hemorrhage and neurologic decline had been confirmed. Based on careful consideration of the radiographic severity of ICH, clinical severity of heart failure, and the patient's neurologic examination, the most appropriate course of treatment was determined: observation alone, observation with suspension of anticoagulation, observation with reversal of anticoagulation, or reversal of anticoagulation plus surgical intervention.

Every patient with ICH received anticoagulation with warfarin leading up to the time of diagnosis. The international normalized ratio (INR) was used to evaluate therapeutic levels of warfarin. The goal range of INR was 2—3. Reversal of warfarin, if necessary, was performed with FFP, PCC, vitamin K, or some combination thereof with a goal INR of <1.4. A diagnosis of AvWD was made based on absence or decreased levels of vWF multimers. An additional test that can be used is the platelet function analyzer (PFA-100; Siemens Medical Solutions USA, Inc., Malvern, Pennsylvania, USA). This is an aperture closure test that evaluates platelet function in the presence of high shear forces similar to those present in a physiologic environment. Citrated whole blood is exposed to high shear forces within a cartridge containing platelet agonists of either collagen and epinephrine or collagen and adenosine diphosphate. Prolongation of the collagen and epinephrine and collagen and adenosine diphosphate closure times has been associated with AvWD and is used at our institution as part of diagnostic evaluation in patients with mechanical circulatory support.[14,15]

RESULTS

Demographics and Clinical Findings

During 2013—2016, 58 patients managed primarily by the cardiothoracic surgery team had previously undergone implantation with an LVAD, TAH, or both. LVADs were implanted in 49 patients, TAHs were implanted in 10 patients, and both were implanted in 1 patient. There were 49 men and 9 women. Spontaneous ICH was diagnosed in 5 patients (8.6%) (Table 1). All 5 patients were men with a mean age of 56.7 years (range, 40—72 years), and all 5 underwent LVAD implantation. The mean time of initial LVAD implantation to a diagnosis of ICH was 32 months (range, 2—84 months). All patients had other significant medical comorbidities in addition to cardiomyopathy and heart failure; however, none had previously known coagulopathies other than regularly taking prescribed oral anticoagulation. All 5 patients were prescribed warfarin as their scheduled anticoagulation regimen. One patient, who was an inpatient at the time of ICH, was on a heparin drip as a bridging therapy to therapeutic warfarin. Four of 5 patients were also taking some form of aspirin with or without dipyridamole.

There were 7 distinct ICHs in 5 patients. The types of ICH included subarachnoid hemorrhage, intraparenchymal hemorrhage (IPH), intraventricular hemorrhage, and subdural hematoma (SDH). Only 1 patient was receiving supratherapeutic warfarin (INR range, 1.6—4) at the time of ICH diagnosis. All 5 patients had AvWD. All patients had a hemoglobin and platelet count within an acceptable range not requiring blood products at the time of ICH.

Intervention

There were 7 surgical procedures performed in 2 patients. Three external ventricular drains (EVDs) were inserted. Two decompressive craniectomies were performed: 1 suboccipital craniectomy for evacuation of a right cerebellar IPH and 1 right hemispheric craniectomy for evacuation of an iatrogenic SDH. The patient with a right hemispheric craniectomy subsequently underwent cranioplasty. One ventriculoperitoneal shunt was inserted for persistent hydrocephalus. Two patients were given FFP and vitamin K for reversal of warfarin. Anticoagulation was discontinued (without reversal) in 3 patients with a goal INR in the therapeutic range. A goal INR of <1.4 was necessary if surgical intervention was expected.

Complications and Outcome

Complications related to placement of an EVD occurred in 2 patients. One patient had intraventricular hemorrhage with EVD tract hemorrhage after placement that was clinically inconsequential, and the other patient had a hyperacute SDH after EVD placement requiring emergent evacuation. There was 1 incident of acute LVAD failure owing to thrombus formation 4 weeks after discontinuing anticoagulation that required device replacement. There were no ischemic strokes after cessation of anticoagulation during the follow-up period.

After treatment, 2 patients had little or no neurologic deficits with a modified Rankin Scale score of 1 and 2, respectively. Mortality rate was 60%. One patient died shortly after presentation without intervention after discovering a massive right hemispheric IPH. The other 2 deaths occurred in patients after long hospital stays with various surgical treatments of ICH.

Illustrative Cases

Patient 2. A 39-year-old man initially presented to an outside hospital with severe headache and dizziness. He underwent LVAD implantation 2.5 years previously. CT scan of the head revealed a right cerebellar IPH with hydrocephalus (Figure 2A and B). An EVD was inserted after his INR of 4.0 was reversed to 1.4. EVD insertion was complicated by a small intraventricular hemorrhage that did not result in clinical sequelae (Figure 2C). The patient arrived intubated and was following commands in all extremities equally, but 3 days after presentation he experienced an acute neurologic decline. He was taken for emergent suboccipital craniectomy with evacuation of the right cerebellar IPH (Figure 2D). He recovered well neurologically, and his hydrocephalus resolved. A diagnosis of AvWD was made

Table 1. Demographics and Clinical Data in 6 Patients with a Left Ventricular Assist Device and Intracranial Hemorrhage

Patient	Age (Years)/Sex	Presenting Symptoms	Hemorrhage Pattern	Classification*	Surgical Intervention	Anticoagulation	Hemoglobin (g/dL)	Platelets ($\times 10^9$/L)	INR	Reversal Agent	AvWD	mRS/ Follow-Up mRS	Complications	Months After LVAD Implant
1	62/male	Seizure	SAH	A	None	Warfarin, ASA, dipyridamole	9	107	1.9	None	+	1/0	None	59
2	39/male	HA, dizziness	IPH	C	EVD, craniectomy	Warfarin, ASA, dipyridamole	11.6	288	4	FFP, VIT K	+	2/6	EVD tract hemorrhage and IVH, LVAD thrombus	36
3	48/male	Altered mental status	SAH, SDH, IVH	C	EVD × 2, craniectomy, VP shunt, cranioplasty	Warfarin, ASA, Heparin gtt	8.1	279	1.6	FFP, VIT K	+	3/6	SDH after EVD, shunt failure with IVH	2
4	64/male	HA, lethargy	IPH, IVH	C	None	Warfarin, ASA, dipyridamole	13.3	326	3	FFP, VIT K	+	5/6	None	5
5	72/male	HA, limb ataxia, visual deficit	IPH	B	None	Warfarin	8.8	194	2.5	FFP, VIT K	+	2/1	None	84

Laboratory values, anticoagulation regimens, and mRS scores were obtained at the time of ICH diagnosis.

INR, international normalized ratio; AvWD, acquired von Willebrand disease; mRS, modified Rankin Scale; LVAD, left ventricular assist device; SAH, subarachnoid hemorrhage; ASA, aspirin; HA, headache; IPH, intraparenchymal hemorrhage; EVD, external ventricular drain; FFP, fresh frozen plasma; VIT K, vitamin K; IVH, intraventricular hemorrhage; SDH, subdural hematoma; VP, ventriculoperitoneal; gtt, drops.

*See Figure 5 for classifications.

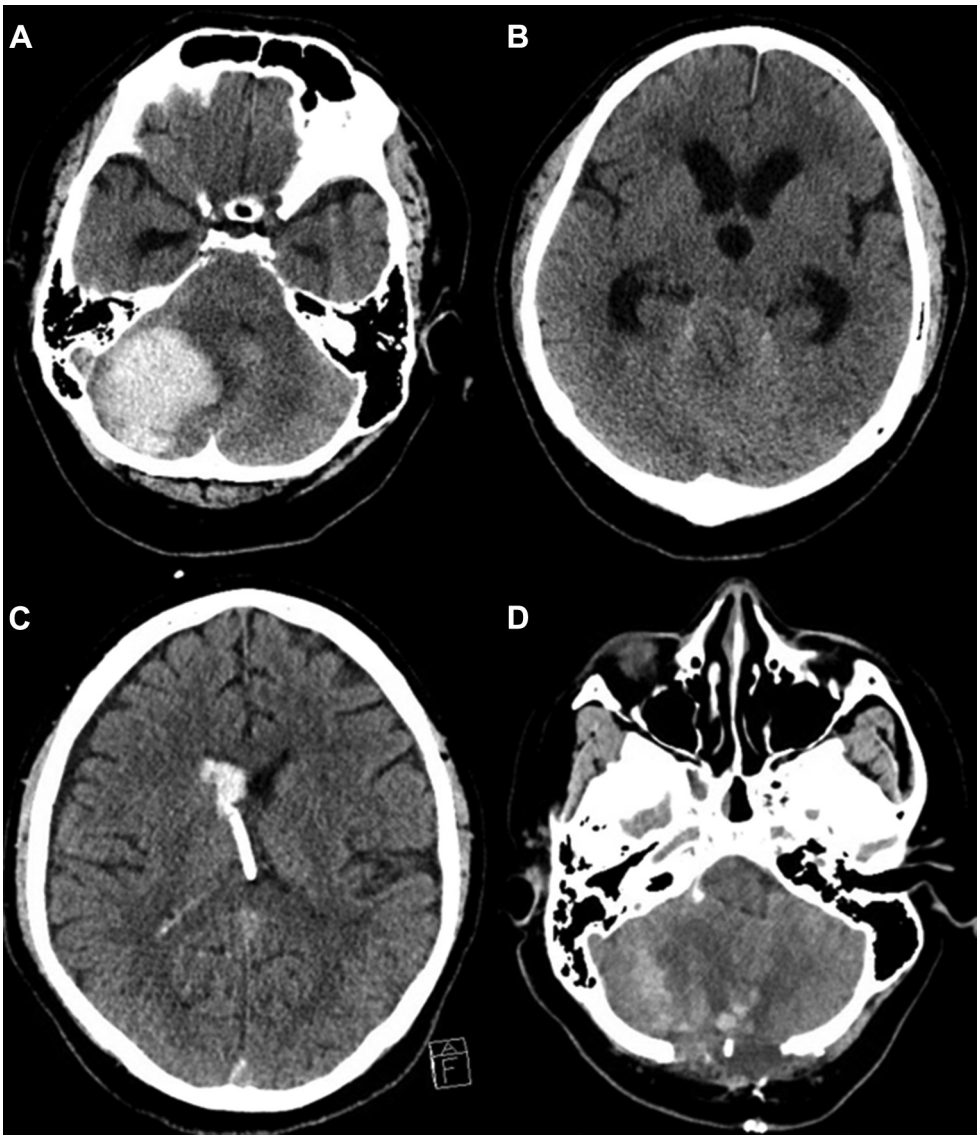

Figure 2. Patient 2. (**A** and **B**) A 39-year-old man presented with a right hemispheric cerebellar intraparenchymal hemorrhage and hydrocephalus on computed tomography scan. (**C**) Insertion of an external ventricular drain was complicated by a small intraventricular hemorrhage. (**D**) Acute neurologic decline on hospital day 3 led to emergent suboccipital decompression with evacuation of the right cerebellar intraparenchymal hemorrhage.

postoperatively based on his platelet function analyzer results. He was ultimately discharged a little more than a month after craniectomy with discontinuation of warfarin and aspirin.

About 6 weeks after discharge, the patient was readmitted for LVAD failure owing to thrombus, which required replacement by the cardiothoracic team. Anticoagulation had not been restarted at this point. He had multiple subsequent wound infections. Ultimately care was withdrawn after sepsis and multisystem organ failure were diagnosed.

Patient 3. A 48-year-old man underwent elective implantation of an LVAD, which was complicated postoperatively with multiple cardiorespiratory issues. About 1.5 months after LVAD placement, the patient experienced acute altered mental status. CT scan of the head revealed a subarachnoid hemorrhage within the basilar cisterns, lateral ventricle intraventricular hemorrhage, and acute hydrocephalus (Figure 3A and B). INR at the time of neurosurgery consultation was 1.6. He was on a heparin drip bridging to therapeutic warfarin and aspirin; these were discontinued in

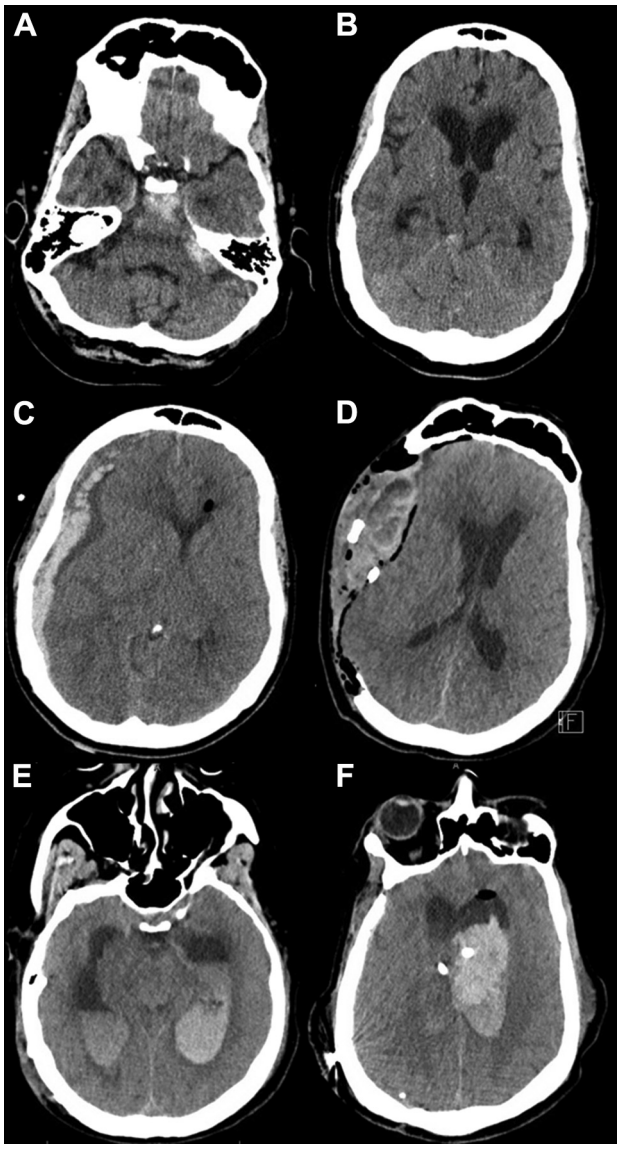

Figure 3. Patient 4. A 48-year-old man experienced spontaneous altered mental status 1.5 months after undergoing left ventricular assist device implantation. (**A**) Computed tomography scan of the head revealed a subarachnoid hemorrhage of the basal cisterns. (**B**) He developed hydrocephalus 1 month later, and (**C** and **D**) an external ventricular drain was inserted, which was complicated by a hyperacute subdural hematoma requiring a right decompressive craniectomy and subdural hematoma evacuation. (**E** and **F**) He returned months later with spontaneous intraventricular hemorrhage that led to shunt failure and death.

anticipation of a possible cerebrospinal fluid diversion procedure. His neurologic examination was improving, and multiple repeat CT scans were stable, so surgical intervention was not performed at that time. He remained neurologically at his baseline for 2 weeks and was restarted on a heparin drip as a bridge to therapeutic warfarin.

About 1 month after initial consultation, the patient experienced altered mental status again, which was attributed to his persistent signs of hydrocephalus on CT. An EVD was inserted after his INR was corrected to <1.4, which was complicated by an acute SDH requiring emergent hemicraniectomy and evacuation (Figure 3C and D). The patient made a good recovery and subsequently underwent an uncomplicated right cranioplasty and ventriculoperitoneal shunt insertion. All anticoagulants had been discontinued indefinitely after testing positive for AvWD in the presence of multiple neurologic and nonneurologic hemorrhagic complications.

The patient presented to the emergency department 12 months after cranioplasty and ventriculoperitoneal shunt insertion with confusion, unsteady gait, and new massive intraventricular hemorrhage with hydrocephalus (Figure 3E and F). His INR at this point was 1.2, and an EVD was inserted in an attempt to drain blood from the lateral ventricles. After 1 week in the intensive care unit with little radiographic improvement and a declining neurologic examination, the patient's family elected to withdraw care.

Patient 5. A 72-year-old man who underwent LVAD implantation 56 months previously presented to the emergency department with a 1-week history of left arm dyscoordination, right hemianopsia, and headache. CT scan of the head revealed a left parieto-occipital and right frontal IPH (Figure 4A and B). He was prescribed warfarin, and his INR at presentation was 2.5. Physical examination revealed a right homonymous hemianopsia and a left upper extremity drift with intact strength grossly.

Although the patient's neurologic symptoms were relatively mild, the left parieto-occipital hemorrhage was large, and therefore warfarin was reversed with FFP and vitamin K to an INR of 1.7. He also tested positive for AvWD. The patient was admitted initially to the intensive care unit to closely monitor his neurologic status, which remained stable throughout his hospital stay. He was ultimately discharged home with an INR of 1.7 at the time of discharge. Warfarin was discontinued and was not restarted until approximately 16 weeks after the ICH, as he had a subsequent gastrointestinal bleed as well. There were no thrombotic complications. His vision slowly improved, with only intermittent blurry vision. Follow-up CT scan of the head revealed resolution of IPHs with encephalomalacia in the left parieto-occipital region (Figure 4C and D).

DISCUSSION

Patients with advanced systolic heart failure and implantable circulatory devices are at high risk for multiple perioperative complications. Patients with LVADs are particularly at risk for spontaneous ICH. Paradoxically, both thromboembolism and spontaneous major hemorrhage are common after LVAD implantation. Therefore, it is not surprising that ICH is a feared and detrimental diagnosis after LVAD implantation. Spontaneous ICH occurred in patients with LVADs at a rate of 8.6% at our institution; this rate is consistent with rates of other studies, which ranged from 8% to 11%.[6,16] Anticoagulation regimens and AvWD combine to render patients with LVADs unusually coagulopathic. Spontaneous ICH occurs across all INR ranges in patients receiving warfarin after LVAD implantation.[17] Similarly in

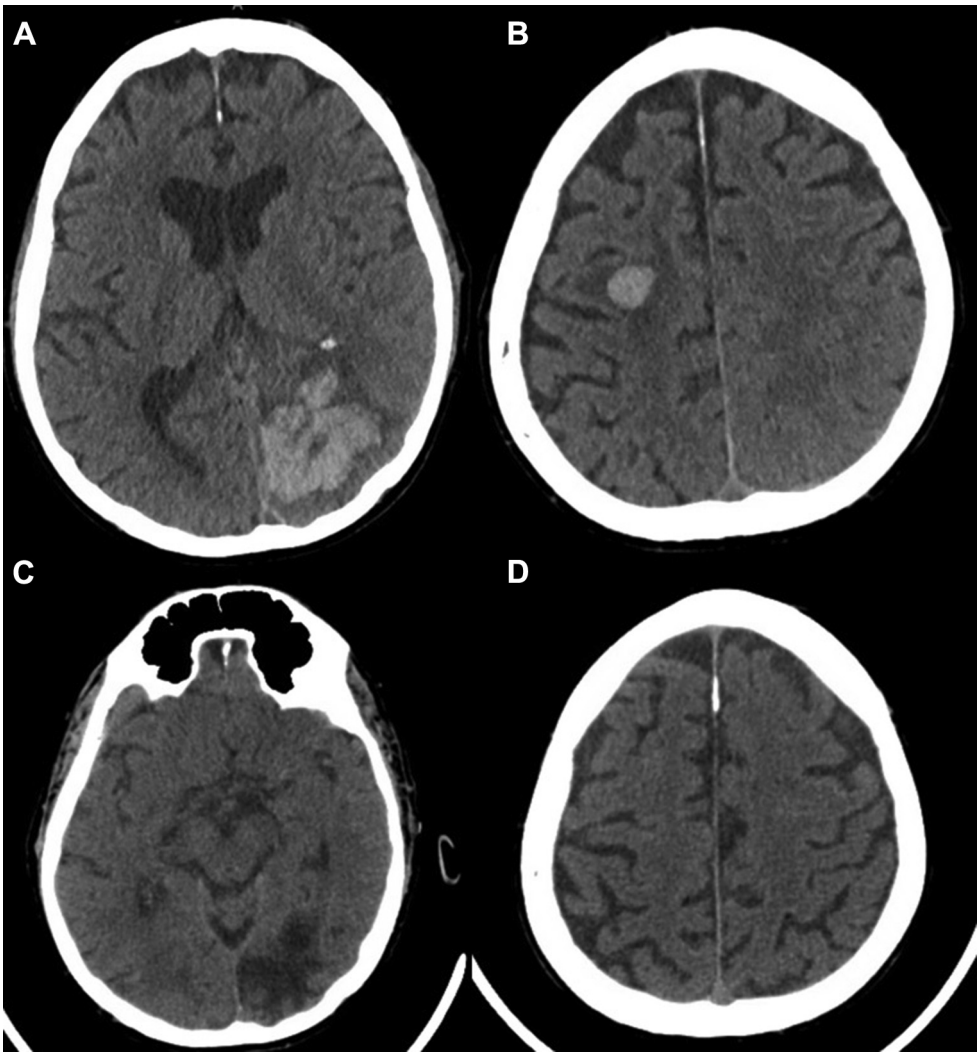

Figure 4. Patient 6. A 72-year-old man presented with a 1-week history of left arm dyscoordination, right hemianopsia, and headache. (**A** and **B**) Computed tomography scan of the head showed subacute left parieto-occipital and right frontal intraparenchymal hemorrhages. Anticoagulation was stopped, and his international normalized ratio was closely monitored. (**C** and **D**) Follow-up computed tomography scan revealed resolution of the intraparenchymal hemorrhages with resultant encephalomalacia in the left parieto-occipital region.

the present study, there was no correlation between elevated INR and the incidence or severity of ICH, as only 1 of 5 hemorrhages (20%) were associated with a supratherapeutic INR. All 5 patients tested positive for AvWD, and it has been shown that in patients who eventually undergo heart transplant after LVAD implantation, hemorrhagic complications decrease as high-molecular-weight vWF levels normalize, confirming the role of AvWD in major bleeding events in patients with an indwelling LVAD.[12]

There is no acute treatment of AvWD other than discontinuation of antiplatelet medications or optimization of modifiable factors such as INR. Several agents, such as factor VIII concentrates, desmopressin acetate, and recombinant factor VIIa, have been used in an attempt to effectively treat AvWD, but the underlying lack of aggregation of large multimer vWF is still not specifically corrected.[18] An intermediate-purity vWF/factor VIII concentrate (Haemate P/Humate-P; CSL Behring, King of Prussia, PA) is a compound that has been used to treat AvWD and contains physiologic aggregations of multimeric vWF, but it has also been associated with device thrombosis.[18] The administration of platelets is not routinely recommended directly after the diagnosis of AvWD is made in patients not requiring surgical intervention, especially considering that it has recently been associated with worse outcome in patients taking antiplatelet

agents who experience spontaneous ICH.[19] However, an exception should be made when a patient is planning to undergo neurosurgical intervention.

After encountering multiple ICHs after LVAD implantation, we have developed a novel algorithm for the management of acute ICH in patients with durable mechanical circulatory support devices (Figure 5). If ICH is suspected, a thorough work-up should be done that includes CT scan of the head and basic laboratory tests, with particular emphasis on the patient's hematologic values. After a radiographic diagnosis of ICH is made, balancing the patient's acute neurosurgical issues with the fragile cardiac condition is of utmost importance. Therefore, we recommend immediately separating patients with absent or only mild neurologic deficit (i.e., dysarthria, mild disorientation, single controlled seizure) from patients with major neurologic deficit (i.e., severe hemiparesis or hemiplegia, stupor, aphasia).

If little or no deficits are present and the INR is within therapeutic range with a small ICH (e.g., IPH <3 cm, SDH <1–2 mm thickness, thin subarachnoid hemorrhage), reversal of anticoagulation is not recommended, and the patient should be monitored clinically and with repeat CT scan of the head 4–6 hours after diagnosis. If the INR is supratherapeutic with evidence of a small ICH, warfarin should be paused with the INR allowed to decrease naturally within therapeutic range while following with serial laboratory studies (class A). These patients should continue anticoagulation and/or antiplatelets, and no outpatient follow-up CT scan is necessary.

If a larger ICH is discovered on CT in a patient with little or no neurologic deficit, anticoagulation should be actively reversed with PCC, FFP, or vitamin K to avoid neurologic decline (class B). Warfarin may be reversed with either PCC or FFP, but PCC may be more beneficial in cases of neurologic emergencies owing to its faster administration in smaller volume. Vitamin K should be given only in the acute phase of the hemorrhage so as not to complicate readministration of anticoagulation. Patients with major neurologic deficit attributable to a large ICH, hydrocephalus, or a combination of ICH and hydrocephalus should be quickly identified and anticoagulation appropriately reversed. Once identifiable coagulopathies are appropriately treated and platelet administration has begun, any neurosurgical interventions should be performed as indicated, while continuing to follow hematologic parameters postoperatively (class C). As AvWD is largely a result of platelet dysfunction, administering platelets at the start of any procedure is recommended to help reduce the incidence of hemorrhagic complications. None of our patients received platelets at the time of surgery because this is a recommendation based on findings within the present study.

Clinical decision making should occur in conjunction with a cardiothoracic surgeon or intensivist. Reversal of anticoagulation as well as the duration of maintaining a subtherapeutic INR is not a benign intervention in patients with LVADs, as evidenced by the successful prevention of stroke using warfarin in patients with atrial fibrillation.[20-22] Similarly, treatment with warfarin has been found to significantly diminish thromboembolic events and device failure owing to thrombosis in patients with an LVAD.[17] For this reason and because other independent thromboembolic risk factors are often prevalent in these patients, discontinuation or reversal of anticoagulation should be done with the cardiac team only after the neurologic and cardiac risks have been collectively assessed. Data suggest that discontinuation of anticoagulation after ICH for a duration of 1–2 weeks in patients taking warfarin for atrial fibrillation or a prosthetic heart valve yields only a 3% 30-day risk for thromboembolic events, but patients with LVADs are generally less healthy and may be even more

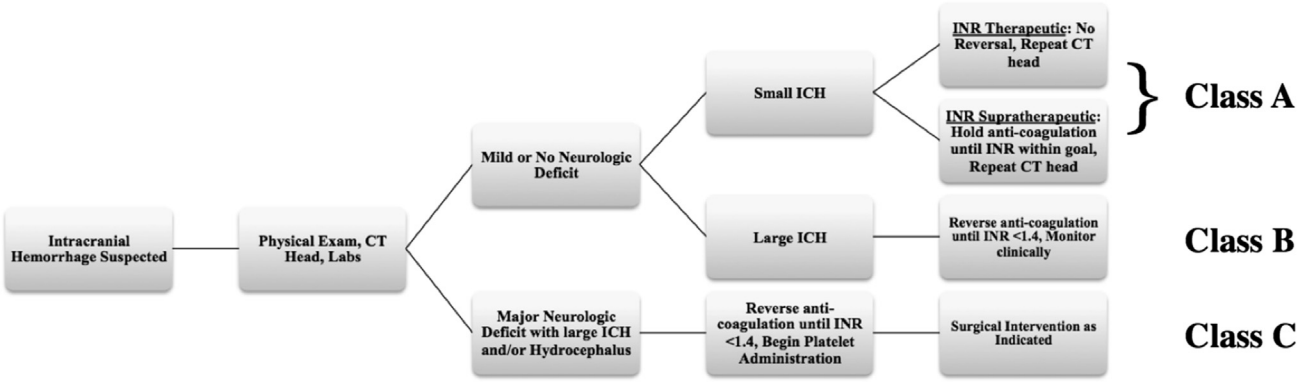

Figure 5. Treatment algorithm for intracranial hemorrhage (ICH) in patients with a left ventricular assist device. After suspicion of ICH is confirmed with computed tomography (CT), patients must be quickly classified as with or without major neurologic deficit. In patients with mild or no neurologic deficits, management is dictated by the extensiveness of the hemorrhage. A large ICH must be managed with reversal of anticoagulation with fresh frozen plasma and/or prothrombin complex concentrate (whichever is more frequently used at the institution), whereas a small ICH should be conservatively managed with observation alone or observation and allowing the international normalized ratio (INR) to passively fall back within therapeutic range. In patients with a major neurologic deficit, surgery can be safely performed after coagulopathies are corrected. When necessary, anticoagulation should be stopped for 2 weeks after neurologic stabilization.

Table 2. Management Based on Classification of Intracranial Hemorrhage and Presence or Absence of Acquired von Willebrand Disease

	Class A	Class B −AvWD	Class B +AvWD	Class C −AvWD	Class C +AvWD
ASA	Continue	Continue	Discontinue	4 weeks	Discontinue
Warfarin	Continue	1 week	2 weeks	4 weeks	4 weeks
Head CT	NA	2 weeks	3 weeks	4 weeks, 5 weeks	4 weeks, 5 weeks
INR goal	2.0–3.0	1.5–2.5	1.5–2.5	1.5–2.5	1.5–2.5

Management algorithm for restarting or discontinuing anticoagulation, obtaining follow-up head CT scan, and following INR goal.
AqWD, acquired von Willebrand disease; ASA, aspirin; CT, computed tomography; INR, international normalized ratio.

dependent on these agents.[23] In our series, 1 patient experienced device failure owing to thrombosis requiring LVAD replacement 4 weeks after anticoagulation was discontinued, thus highlighting the careful consideration with which anticoagulation regimens should be managed.

Table 2 outlines recommendations based on our experience for managing anticoagulation in these patients as an outpatient after diagnosis of ICH. Patients with class A ICHs may resume anticoagulation without neurologic follow-up. Aspirin should be discontinued indefinitely in patients with AvWD, as the diagnosis is representative of inherent platelet dysfunction. Patients with class B and C ICHs without AvWD should under a CT scan of the head 1 week after restarting warfarin. Patients with AvWD should undergo a CT scan of the head at the time of restarting warfarin and again 1 week later. All patients with class B and C ICHs should have a lower INR goal than before ICH, with a goal of 1.5–2.5.

Although surgery can be safely performed after correction of reversible coagulopathies, extra care must be taken in the perioperative phase to reduce the risk of procedure-related hemorrhage. Even with an INR <1.4, platelets >100 × 10^9/L, and an otherwise normal hematologic profile, one such complication occurred in this series following a ventriculostomy resulting in an acute SDH requiring evacuation. It was later discovered that this patient had AvWD, and this is the first neurosurgical procedure complicated by AvWD in the literature. As AvWD is a disease of platelet dysfunction, when a surgical intervention is planned, we recommend giving platelets just before the start of the procedure to minimize surgical hemorrhagic complications, which occurred in both patients requiring surgery in the present study. Nevertheless, we do not think AvWD should prevent neurosurgical intervention in cases of neurologic emergency once all other hematologic variables have been appropriately addressed.

CONCLUSIONS

For the first time in the neurosurgical literature, we describe the nature of ICH as a result of the bleeding risk associated with LVADs and AvWD. Management of ICH is unusually complex in these patients because of their tenuous condition as a result of multiple coagulopathies, risk for thromboembolism, and their preexisting cardiac status. In the face of potentially irreversible neurologic injury, neurosurgeons must balance aggressively treating ICH both medically and surgically with the complex hemodynamic and global risk factors present in patients with LVADs. We propose a novel treatment algorithm for such cases, which must be implemented in a multidisciplinary manner to best avoid both neurologic and cardiovascular complications.

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