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System Proposal for Supervision of Critical Adverse Processes in Patients with Implanted Ventricular Assist Devices

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Abstract: Ventricular assist devices (VADs) are designed to provide sufficient blood flow to patients with severe heart failure. Once implanted, the patient becomes dependent on the VAD, making it essential to prevent situations that could harm the patient while receiving circulatory support. VADs are classified as critical systems (CS), and adverse events (AEs) can lead to serious consequences, including hospitalization or even death. At present, patient care is provided through in-person consultations, with incidents reported via medical device reports (MDRs) to the Food and Drug Administration (FDA). However, there is no real-time monitoring of AEs or oversight of these events. In response to this gap, a system for supervising critical adverse processes in patients with implanted VADs (SCVAD) is proposed, based on horizontally and vertically integrated architecture. This system aims to address the complexity of AEs by considering multiple domains of operation: the device, the patient, and the medical team, as well as the interactions between these entities. In this context, the formalism of Petri nets (PN) is used to develop models that represent adverse processes based on the actions recommended by the medical team. These models allow for the mapping of events with the potential to cause harm to the patient. Therefore, the medical team will be able to monitor adverse processes, as the models in interpreted PN can be isomorphically transcribed into computable algorithms that can be processed on compatible devices, enabling the tracking of complications caused by adverse processes.

Keywords: ventricular assist device; adverse event; petri nets

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1. Introduction

Ventricular assist devices (VADs) are life support mechanisms for patients with heart failure (HF). According to the American Heart Association (AHA), HF is a chronic and progressive condition in which the diseased organ cannot pump enough blood to meet the body's demands for oxygen and nutrients [1]. One of the treatment options for such cases is the use of VADs [2–5]. One indication for these devices is to assist the left ventricle of the patient's heart when the disease impairs it and it cannot meet the physiological demands of the cardiovascular system to supply the body's needs [6–9].

Ventricular assist devices (VADs) are recommended for use, involving three different objectives: use as a bridge to transplant (BTT) to maintain circulation at physiological levels until a transplant can be performed; use as a bridge to recovery (BTR) uses devices for myocardial recovery; or use as a destination therapy (DT) when the patient is not eligible for a transplant [2,3,7].

In cases where the implantation of a VAD is indicated, it is essential to clarify that the patient becomes entirely dependent on the proper functioning of the device to maintain their blood circulation [2–5]. In this context, failures may occur that compromise the VAD's functionality, a topic that has been extensively researched [8–11]. Furthermore, there is the possibility of adverse events (AEs) associated with the use of these devices, which requires

solutions to address these occurrences and their consequences, which can potentially lead to life-threatening risks for patients with VADs.

Examples of complications associated with these AEs include infection, thrombosis, bleeding, arrhythmias, right ventricular failure, and stroke, which can result in immediate harm to the patient [12,13]. For this reason, VADs are classified as critical systems (CS) due to the high dependency of the patient on their proper functioning and the potential for them to cause AEs that can be fatal [8,11].

In the context of a patient with an implanted VAD, the critical element is the human factor, and depending on the undesirable situations that may arise, recurrent hospitalizations can be triggered, as well as a risk of death for a specific patient profile due to the damage caused by the occurrence of adverse events [13,14]. Therefore, the supervision of the patient's health status is limited by the following factors:

- Possibility of adverse event occurrence.
- Difficulty in identifying the occurrence of these events.
- Difficulty in diagnosing the progression of adverse processes caused by these events.
- Commercial devices don't provide real-time monitoring of adverse events, and patient supervision is performed in person, during emergency situations, or based on complaints reported by the patients themselves [13–17].
- The circulatory assistance provided by VADs marketed in recent years is managed by a local controller that is not remotely connected to the medical team [15–17].

The objective of this study is to propose a system for supervising critical adverse processes in patients with implanted ventricular assist devices (SCVAD) based on an event-driven modular framework that features both horizontal and vertical integration, as well as timers for tracking the patient care process. To achieve this, diagnostic models for adverse events and intervention models based on intervention protocols determined by competent medical teams were proposed. Therefore, it becomes possible to map the system's undesirable states, which change with each new adverse event. In this context, event-driven models using interpreted Petri nets were proposed, which allow for the representation of events and the current and future states that can be reached during the adverse process, as well as the control of the flow of necessary external information (to the patient with an implanted VAD and the supervising medical team).

In contrast, the intervention models oversee actions the medical team recommends for interrupting an adverse process, linking timed control strategies based on the watchdog concept. The update of the adverse process status is communicated to the medical team so they can monitor the patient's condition and assess which mitigation activities can be carried out to interrupt the adverse process.

The paper is structured as follows: Section 2 describes the complications associated with the use of VADs. Section 3 presents the proposed method and the modeling of SCVAD processes. Section 4 provides models based on an example of adverse events and the results obtained. Section 5 discusses the results, and finally, Section 6 presents the conclusions drawn from the results.

2. Related Works

This section is divided into three subsections. The first subsection provides context on adverse events (AEs) and the risks associated with them. It also presents the effects of AEs and how they are managed in patients. The second subsection discusses the complex characteristics of the system, related to the dynamic interaction between the patient with an implanted VAD and the supervising medical team. Finally, the third and last subsection presents the formalism for modeling critical adverse processes using interpreted Petri nets. Petri nets (PNs) are mathematical models that enable the representation of events that cause state changes. Thus, by using techniques for synthesizing PN-based models, it is possible to identify inconsistencies and validate them through simulators [18–21]. These validated PN models can then be isomorphically transcribed into computable algorithms for programming the SCVAD [22].

2.1. Adverse Events

An AE can be defined as an incident that results in unintended harm, arising from the care provided by a medical device, and which is not necessarily related to the natural progression of the patient's disease. The harm caused by AEs can lead to prolonged hospitalization or readmission, disability, permanent damage, or death [13,23]. Some of the likely AEs include bleeding, thrombosis, pulmonary embolism, stroke, infection, and VAD malfunction associated with coagulation [24].

It is well known within the medical community that an increased risk of arrhythmias is associated with the implantation of VADs. Although arrhythmias are AEs that can be managed and their effects can be minimized with drugs and/or medical interventions, if persistent, they may lead to hemodynamic disturbances, right ventricular failure, and organ dysfunction. The complications associated with arrhythmias can also result in recurrent hospitalizations and involve a risk of death or dangerous combinations of AEs [12].

Between 2008 and 2015, recurrent cases of thrombosis in VADs were reported, resulting in an increase in hospital readmissions due to complications associated with AEs, including surgeries for device removal or replacement and, in some cases, death [25–27]. To identify the presence of thrombosis, techniques for measuring the vibrational performance of the pump can be used, which allow for monitoring potential anomalies in the device's operation caused by the presence of thrombi attached to the rotor [28,29].

The follow-up of patients with an implanted VAD is carried out through consultations and medical exams. Medical Device Reports (MDRs) are part of this process. The Food and Drug Administration (FDA) is the regulatory agency responsible for the evaluation of drugs, medical devices, and, more generally, almost everything related to public health in the United States of America. It is the agency to which pharmaceutical and medical device manufacturers submit their requests for commercial approval. It also reviews voluntary and surveillance reports, known as MDRs, which include reports of malfunctions, serious injuries, or suspected deaths associated with the use of medical devices. The FDA's database consolidates information on various reports, including patient harm due to AEs, harm caused by failures or defects in medical devices, as well as usage guidelines, and recalls are also published [23,30,31]. MDRs are submitted by medical centers based on complaints reported during treatment or by observations from the patients themselves, who are aware of the effects caused by the AEs. Although the patient is followed by the medical team, there is no real-time monitoring of the VAD, which may lead to delayed identification of AEs, given that in-person medical evaluation is required [16,17,30,31].

Table 1 presents a compilation of MDRs for complications associated with AEs over the last four years. The observed percentage was calculated based on the total number of annual MDRs presented as follows: 2021 (71,882), 2022 (49,358), 2023 (25,311), and 2024 (5958) [23].

Table 1. MDRs mentioning AEs submitted to the FDA in the last four years.

Adverse Event	2021 (MDRs)	2021 (%)	2022 (MDRs)	2022 (%)	2023 (MDRs)	2023 (%)	2024 (MDRs)	2024 (%)
Infection	7863	10.9	5817	11.8	2758	10.9	581	9.8
Thrombosis	2941	4.1	1836	3.7	915	3.6	194	3.3
Bleeding	2944	4.1	1778	3.6	799	3.2	178	3
Renal dysfunction	1583	2.2	970	2	364	1.4	82	1.4
Stroke	1588	2.2	1081	2.2	536	2.1	112	1.9
Hepatic dysfunction	1837	2.6	1210	2.5	633	2.5	131	2.2
Heptic dysfunction	306	0.4	197	0.4	88	0.3	16	0.3

Between 2015 and 2019, the occurrence of 'early AEs' was the main complication in the postoperative period, occurring within the first 90 days after implantation and

potentially extending to 12 months of treatment as 'late AEs'. During this period, bleeding and infection were the most common causes of hospital readmission [32,33]. A recent case illustrates the relevance of this issue: on 3 June 2021, Medtronic discontinued the sale and commercial distribution of the HVAD device, although it continues to provide care to some patients already using the device. However, new implants were suspended, and the device is being gradually withdrawn from the market due to evidence of increased mortality associated with AEs [34].

2.2. Complexity of the System: VAD, Patient, and Medical Team

One of the fundamental characteristics for identifying complexity in systems is emergent behavior [35–37]. Therefore, the approach to solving problems in complex systems (CS) cannot rely on solutions that consider well-defined, restricted problems with known solution paths and convergent answers. Instead, an approach that can handle the challenges imposed by these systems is more recommended [38]. According to Piqueira [36], CSs have a particular behavior of interacting with the external environment, being classified as open systems. These interactions lead to changes in the global behavior of the system, which are linked to another characteristic of complexity, adaptation and resilience, in response to external changes [35–37].

Considering the use of VADs, the influence of the external environment is observed, especially in response to stimuli generated by changes in physical activity. For example, during physical exertion, the increased metabolic demand requires VAD controllers to adjust blood flow to ensure adequate circulatory support. This highlights the importance of effective integration between the VAD operation and the hemodynamic behavior of the system, as discussed by Leao et al. [39] and Santos et al. [40].

An important characteristic of complexity in VADs is their dynamic interaction with the cardiovascular system, which has its own control mechanisms [13,41,42]. Therefore, the VAD operates within a complex system, where the regulation of the heart rate and respiratory rate, as highlighted by Mazzeo [42], is mediated by the actions of the parasympathetic and sympathetic systems, which cooperate to maintain homeostasis. This sophisticated system is essential for ensuring physiological stability.

Based on the context provided regarding patients with an implanted VAD, a complexity is observed resulting from the interaction among three fundamental entities: the VAD, the patient, and the medical team. The following presents some of the characteristics of this system formed by the patient, VAD, and medical team, considering the interactions described and the complexity principles explored in refs. [35,36].

- Interactivity: The system involves the participation of the 'VAD' and its subsystems (blood pump, cannulas, controller, driveline, and power supply), the 'patient' and their various subsystems (composed of organs, tissues, and cells that interact with each other), and the 'medical team', which interacts with the other two elements to monitor and supervise processes that may occur in the patient. The numerous interactions between the elements of the system are a complexity attribute that highlights the impacts of undesirable events. These impacts include both the effects that AEs can have on the functioning of the DAV and the effects on the patient, both involving potential risk.
- Adaptability: The system is dynamic, and behavior changes are driven by interactions between its entities. This attribute is related to other characteristics, such as the influences of interaction with the external environment [37] and the emergence of the system [35]. These dynamics highlight adaptations and self-organization of the elements, resulting in a sophisticated synergy capable of inducing changes in global behavior.
- Non-deterministic: The system's response is unpredictable, and its behavior is stochastic, meaning that the observed phenomena are random. This characteristic is evident in the occurrence of AEs, which emerge unpredictably. There is no predefined sequence nor a way to accurately predict when or which patient will experience a specific AE.

After examining the characteristics of the studied system, the diversity of processes related to the operation domains and interactions between the DAV, the patient's body, and the medical team stands out. Therefore, the system under analysis is considered open, as it continuously communicates with the external environment [37,43] and presents complexity due to the distinctive nature of the interactions between the entities, which include attributes such as emergence and numerous interactions [35,36].

In the context of AEs, these may occur in an unknown sequence, leading to critical adverse processes with the potential to cause harm to the patient. Based on the characteristics of the studied system and the way these events can unfold, there is an additional layer of complexity. Although AEs are known, their prediction and diagnosis are hindered both by the indeterminacy of when they may occur and by the unpredictability of the sequence of subsequent events.

Based on the arguments and complexity attributes discussed by Ladyman [35], Estrada [36], and Piqueira [37], which establish that the sum of the parts does not correspond to the whole, and on the aspects addressed by Sigahi [38], which indicate the shortcomings of adopting reductionist approaches for complex systems, it can be concluded that reductionist approaches will not be effective in dealing with the inherent complexity and dynamic interactions of these systems.

Different contexts may involve distinct interactions between the elements involved; therefore, there are a variety of processes throughout the patient's life cycle with DAV, which will be presented below. The system in question behaves as a discrete-event system (DES), meaning that its state evolution is entirely dependent on the occurrence of asynchronous discrete events over time [44].

In this context, Petri nets (PNs) are presented as a powerful tool for modeling and describing critical adverse processes. This approach allows the representation of events and current and future states that can be reached during the adverse process, as well as the control of information flow between the patient and the implanted DAV and communication with the supervising medical team.

2.3. Formalisms for Process Modeling of Complex Systems

Petri nets (PNs) are formal tools for modeling the behavior of discrete-event systems (DES) [44]. They enable modeling dynamic behaviors involving parallelism, concurrency, asynchrony, and non-determinism [43,45]. Various classes of Petri nets can be applied for process modeling; however, interpreted Petri nets were chosen [18].

Notably, the production flow schema (PFS) is a high-level unmarked class of Petri nets, known as channel agency nets [19], designed to address the limitations of 'one-step design' techniques for modeling complex systems. The PFS allows for the graphical representation of processes as sequences of steps that represent activities interconnected through distributor elements.

In this context, the PFS is a bipartite graph composed of activity elements (active elements capable of performing transformations, such as actions or task execution), distribution elements (passive elements that do not perform transformations but can collect, accumulate, store, and distribute items), and directed arcs to connect the 'activity' and 'distributor' elements. A graphical representation of the essential elements that make up a PFS graph is presented in Figure 1.

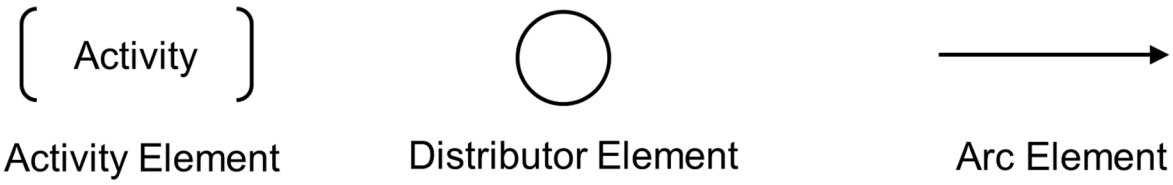

Figure 1. Essential elements of a PFS graph. The square brackets represent the 'activity' element, the circle represents the 'distributor' element, and the arrow represents the 'arc' element.

The PFS diagrams serve as a basis for generating models of various classes of PNs [20], such as the interpreted PNs mentioned earlier [18]. Each activity in a PFS can be detailed into elements of a PN, represented as follows. Figure 2 (starting from A) presents an initial activity of the PFS, which will be further detailed using a condition-event Petri net, for example.

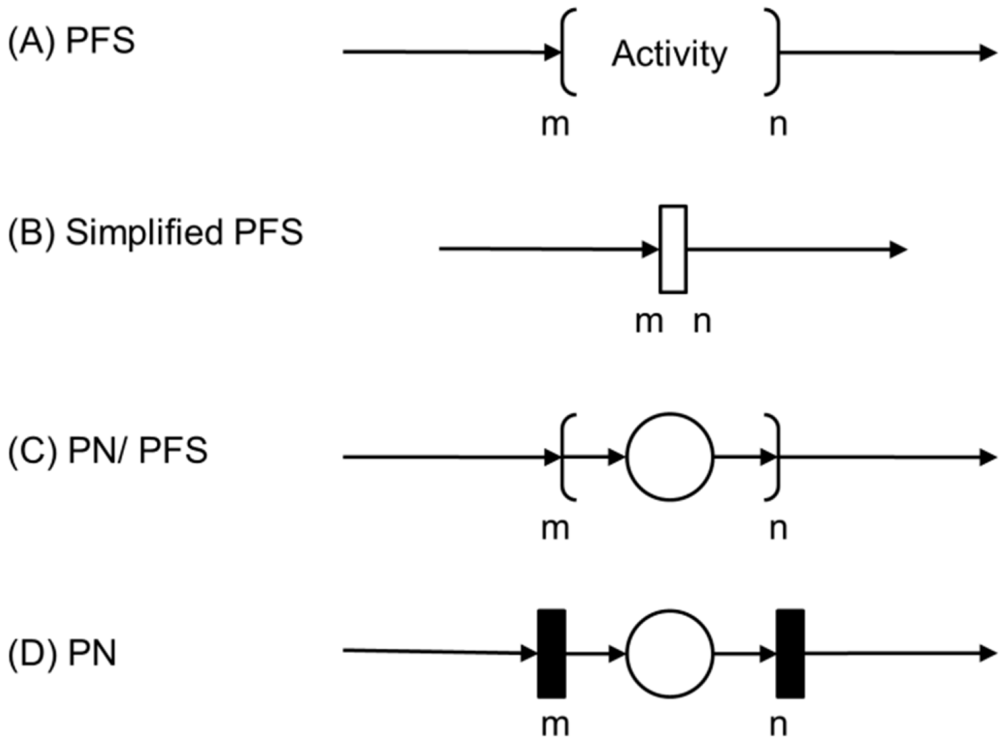

Figure 2. Conversion of the model from PFS to PN through successive top-down refinement. In (**A**), an activity in PFS; in (**B**), another possible representation of the same activity element; in (**C**), a combined PFS/PN representation (the activity is represented by a discrete place between two discrete transitions); and in (**D**), the corresponding PN is represented.

To illustrate the procedures for modeling critical adverse processes, a PFS model of a process is proposed in Figure 3, which is initiated by the action of an external element and requires a resource to perform the processing.

Figure 3. PFS model of the exemplified process.

Figure 4 shows the detailed activity of the 'process' in a corresponding PN using the PFS/PN methodology.

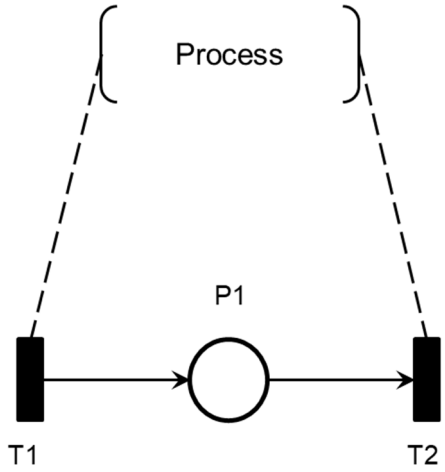

Figure 4. Detailed process model in PN.

In Figure 4, the 'process' activity is detailed in a corresponding PN using the procedures for converting models from PFS to PN (which were described earlier in Figure 2). This approach is repeated for all processes throughout the text and is represented in the figure by two dashed lines. The elements T1 and T2 of the PN represent discrete transitions triggered by events, while the circle P1 represents a discrete place where activities are processed. In Figure 5, place P0 is the command from the external element, and place P2 represents a specific resource. A token (black circle) in place P0 enables the start of the process, provided there is also a token in P2, indicating that the resource is available.

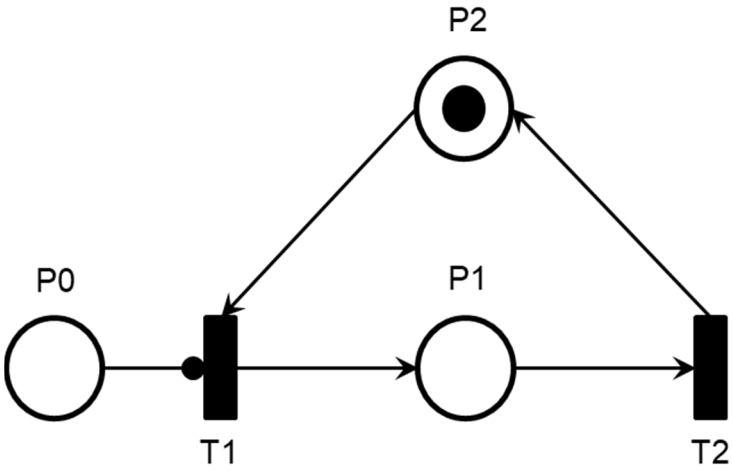

Figure 5. Introduction of resource control elements for sharing.

In Figure 6, the data flow with the external environment is represented. The output S1 indicates the status of the process, which is linked to place P1. Transition T1 can be triggered when there is a token in P0 and another in P2. When triggered, T1 causes a state transition, consuming the tokens from places P0 and P2 and placing a token in P1. A new state transition may occur with a new event. This event will trigger transition T2, which consumes the token from P1 and returns it to P2, indicating that the resource is available again. Therefore, the process can restart when a new token is inserted in place P0 by the action of the external element.

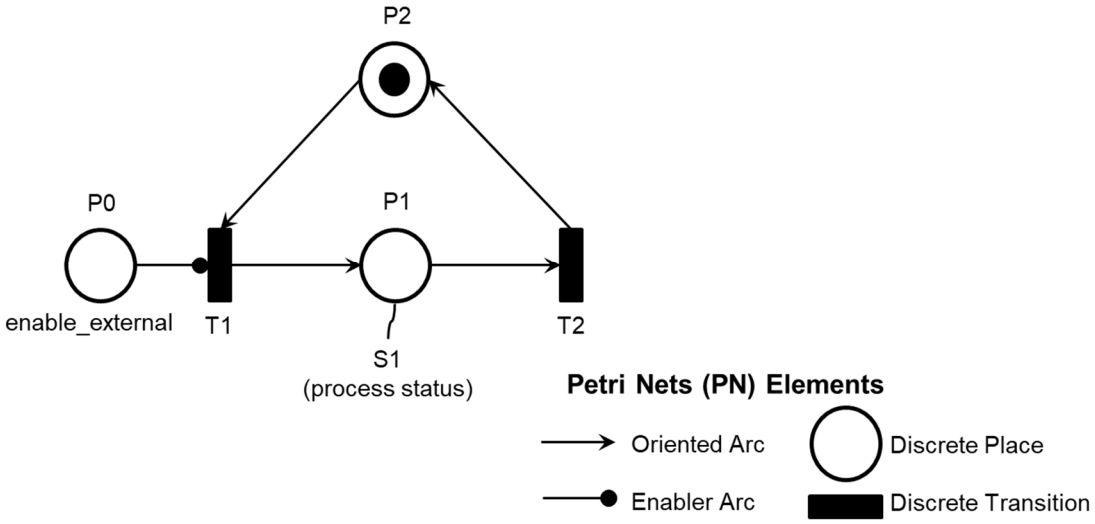

Figure 6. Representation of data flow to the external environment.

3. Proposed Supervision System and Method for Process Modeling

3.1. SCVAD

The proposed system for supervising critical adverse processes in patients with implanted ventricular assist devices (SCVAD) features a structure that enables both horizontal and vertical integration [46,47], which are fundamental characteristics for implementing a system that aligns with the level of complexity present in its dynamic behavior.

Regarding horizontal integration, the structure was designed to support the dispersion between the entities that make up the SCVAD. This structure is configured with a middleware approach to integrate the medical team with the other system entities [46,47]. Additionally, the proposal is based on event-driven architecture (EDA), which facilitates vertical integration between the SCVAD modules and entities, with the aim of providing patient assistance, monitoring AEs, and performing the necessary mitigation activities.

As the architecture is event-driven, the entities interact with each other through the emission and reception of events. Middleware ensures communication between the entities, such as the DAV, the patient, and the medical team, as well as enabling interaction between the various systems outlined in the structure.

The medical team has a module dedicated to diagnosing and tracking the evolution of the adverse process, while another module enables the execution of mitigation activities based on the team's knowledge. This module also allows for specifying the necessary actions to interrupt an adverse process, guiding the execution of mitigation activities effectively.

Figure 7 illustrates three interconnected blocks with bi-directional flow, representing their interaction. The horizontal communication interface between the physical objects corresponding to the VAD entities, patient, and medical team is provided in blue. In green on the left, a modular structure called the digital model for adverse event diagnosis (DMAD) is represented, and each module is developed to identify a specific AE and its consequences. The role of the DMAD is to provide the medical team with two main pieces of information:

- Transitions of undesirable states.
- Timing of adverse processes based on the concept of a watchdog as an estimate of the maximum time required to assist the patient.

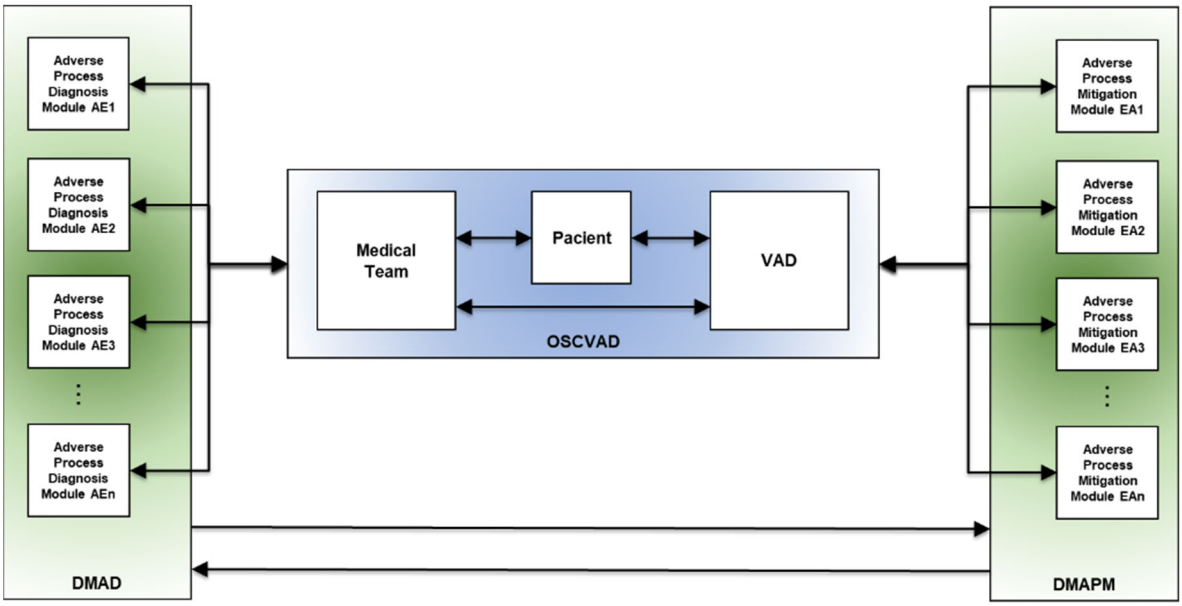

Figure 7. Event-oriented structure model of the SCVAD for digitizing patient care processes.

In green on the right, another modular structure, the digital model for adverse process mitigation (DMAPM), is represented. In each module, mitigation activities for a specific adverse processes are specified. The use of the DMAPM enables three crucial functionalities:

- Supervision of mitigation actions;
- Dynamic monitoring of executed mitigation activities.
- Supervision of mitigation activities that are yet to be executed.

As shown in Figure 7, the function of each item is as follows: the item on the left is the digital model for adverse event diagnosis (DMAD), the item on the right is the digital model for adverse process mitigation (DMAPM), and the item in the center represents the horizontal integration among the entities that constitute the SCVAD.

3.2. Definition of SCVAD Processes

This section defines fundamental aspects of contextualizing critical adverse processes. Initially, in Section 3.2.1, a method for structuring processes involving the domains of operation and interaction among them is presented to delineate different operational contexts defined by regions susceptible to the occurrence of AEs. Subsequently, Section 3.2.2 introduces the necessary steps for modeling adverse processes.

3.2.1. Method for Structuring Processes of the SCVAD

The digital integration of the DAV, patient, and medical team entities requires the development of applications that provide information through the sending of structured events, using application programming interfaces (APIs) and services compatible with EDA, in a publish–subscribe model [46,47]. Through the APIs, communication occurs via the exchange of events or messages, where entities can publish events ('send messages') and others can subscribe to topics to receive these messages. Considering that each entity has autonomous and dynamic behavior, depending on the operational context, it is necessary to highlight the unique characteristics and specific requirements of each one.

(A) The 'VAD', the patient, and the medical team have telemetry resources to enable communication among the entities via an onboard control system or through mobile devices.
(B) The 'patient' has physiological control and regulation mechanisms to maintain homeostasis.

(C) The 'medical team' has the necessary expertise to monitor the patient's progress and conduct appropriate therapeutic interventions, particularly regarding the occurrence of AEs and the complications they may cause.

In this way, it becomes evident that an inherent complexity is associated with the dynamic interaction possibilities among the VAD, patient, and medical team. If reductionist techniques that do not address this dynamic reality are applied, the patient's health status may be compromised, potentially leading to a life-threatening condition.

The model illustrated in Figure 8 was proposed to structure the processes of the SCVAD, delineating different operational contexts of the entities and their interactions. Sets A, B, and C are designated to represent the operational domains of each entity. The numbered regions from 1 to 7 are detailed. The red-highlighted numbering indicates the regions where the context of AEs applies, according to the proposal of this work.

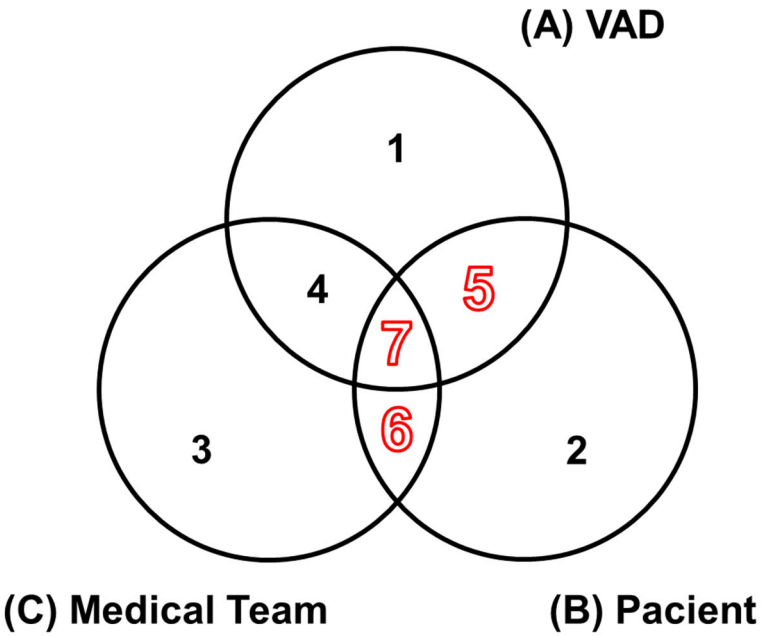

Figure 8. The model for structuring SCVAD processes is represented. Note: The red numbering highlights areas susceptible to AEs (5, 6, and 7), while the black numbering identifies areas unrelated to AEs (1, 2, 3, and 4).

The following describes the seven regions with distinct semantics:

- Region 1: Each element in this region of set A represents processes associated with the VAD in the context of its local control system, including the device for processing embedded control algorithms, sensing devices, actuators, and integration with supervisory systems. Therefore, the concept of AEs does not apply in this region, as events may occur that are associated with potential failures of various natures.
- Region 2: Each element in this region of set B represents physiological processes inherent to the behavior of the patient's cardiovascular system. It is precisely in this context that AEs may occur, and it is essential to note that AEs occurring in this region are not necessarily related to the other entities.
- Region 3: Each element in this region of set C represents issues with the medical team unrelated to the patient; therefore, the concept of AEs does not apply here.
- Region 4: Each element in this intersection region between A and C, without the patient, corresponds to processes involving the proper selection of a VAD for a specific patient profile, as well as the setup of operating conditions according to this profile. Therefore, the concept of AEs does not apply in this context, as the patient is absent.

- Region 5: Each element in this intersection between A and B, without the medical Team, corresponds to processes involving direct interactions between the patient and their VAD, where the concept of AEs applies.
- Region 6: Each element in this intersection region between B and C, without the VAD, corresponds to possible medical interventions by the medical team that involve patient care before the VAD implant or during its use, occurring throughout the patient's life cycle. Therefore, AEs occurring in this region are associated with medication use.
- Region 7: Each element in this intersection region between A, B, and C represents processes involving direct interaction among the entities, meaning that AEs occurring in this region are necessarily linked to the other entities, including the patient, and therefore the concept of AEs applies.

3.2.2. Modeling of SCVAD Processes

The processes are defined within the event-oriented modular structure presented in Figure 3 to address patient needs based on SCVAD specifications. For each process, two modules are specified: one represents the evolution of undesirable states following the occurrence of an adverse event (digitization of the adverse process), while the other focuses on actions recommended by the medical team for mitigating the adverse process. Three steps are planned for specifying modules that meet the requirements of an adverse process: Step 1: Identification of risks associated with the occurrence of an adverse event; Step 2: Development of the adverse process model; and Step 3: Development of intervention protocols.

In Step 1, for identifying risks associated with the occurrence of an AE, one of the techniques that can be utilized is hazard and operability studies (HAZOP), which is used to identify operational problems in a facility or processes [48]. It involves thoroughly investigating each process to find potential deviations based on design requirements and identifying causes and consequences. By identifying the causes and consequences associated with each deviation, actions are specified to eliminate or control the operational hazard in the facility or processes [48]. The HAZOP methodology was developed to meet the needs of projects in the chemical process industry; however, ISO 14971 [49] provides specifications for regulating health-related products and suggests HAZOP, among other techniques, for risk identification involving the use of medical devices. Therefore, the recommendations can be applied to the risk identification study, considering VADs and AEs according to the needs required for this work.

Step 2 refers to modeling the adverse process based on the information obtained in the previous step, which combines specialized knowledge with clinical care protocols and management throughout the life cycle of a patient with an implanted VAD. Models are developed in PFS and then transcribed into PNs to constitute an adverse process diagnostic module specific to each AE and its respective adverse process.

Step 3 involves the development of models that implement intervention protocols based on the risk identification step, where actions recommended by the medical team to interrupt the adverse process are specified. Models are also developed in PFS and then transcribed into PNs to constitute an adverse process mitigation module, which is also specific to each AE and its respective adverse process.

The proposed method can be applied to any AE, with the three steps presented being repeated for each one. In this way, the application of the method proposes models that reflect combined actions, based on specialized knowledge and clinical care protocols, which can implement evidence-based best practices.

4. Use Case

An adverse event is chosen to apply the method, as presented in Section 4.1. To illustrate this, a case example is presented based on clinical practices and the expertise of the medical team, which provided guidance for the diagnosis and treatment of blood flow obstruction caused by thrombosis in a blood pump [25]. Scandroglio et al. [25] provide

information that guides approaches for diagnosing obstruction at three points susceptible to blockage. Additionally, recommended actions by the medical team for the respective necessary interventions are presented.

Section 4.2 presents a risk identification study using HAZOP across three flow obstruction scenarios, namely, 'pre-pump thrombosis', 'intra-pump thrombosis', or 'post-pump thrombosis'. The evaluated parameters and deviations were established, as well as the keywords for identifying causes and recommended actions. It is the prerogative of HAZOP to assemble a team of experts for risk identification; however, this action was not necessary, as all relevant information was provided by Scandroglio et al. [25] and used in filling out the risk identification tables related to blood flow obstruction.

Section 4.3 presents the models for diagnosing the adverse process (AE1) involving the three scenarios, namely, 'pre-pump thrombosis', 'intra-pump thrombosis', and 'post-pump thrombosis'. Following that, a proposed methodology is presented for the development of intervention protocol models, aimed at supervising the mitigation activities of the adverse event (AE1) process, considering the three scenarios mentioned.

4.1. Case: Thrombosis in the Device

Between 2008 and 2015, recurring cases of thrombosis in VADs were causes of hospital readmissions and patient deaths with implanted VADs [25–27]. The reported cases prompted a group of physicians to reflect on best practices for detecting and treating blood flow obstruction in patients with an implanted VAD [25]. Among the previously mentioned complications, thrombosis was chosen for the application of the method because, although it occurs infrequently, it has the potential to cause severe damage that can interfere with the VAD's ability to provide adequate blood flow to the patient, involving an elevated risk of death.

The HVAD was implanted in patients. The device uses a centrifugal pump actuator. The inflow cannula is inserted into the left ventricle, while the outflow cannula directs blood flow to the aorta [15,34]. Considering the potential risks associated with thrombus formation, it is essential to evaluate and establish a method for monitoring these events. Since such events may occur, it is crucial for the medical team to establish diagnostic guidelines and implement the necessary interventions. Therefore, a study is proposed to identify the risks associated with these events and the potential adverse processes that may follow.

It was unnecessary to gather specialists for data collection since the secondary data represents the knowledge and expertise of a team of specialists and meet the needs outlined for this work. Next, the information established by the medical team as inputs for diagnosing blood flow obstruction, taken from Scandroglio et al. [25], is presented.

(1) Indirect measurement of blood flow (acquisition via device alarms).
(2) Indirect measurement of electrical power consumption (acquisition via device alarms).
(3) Direct measurement of pump vibration through acoustic analysis.
(4) Imaging diagnostics through exams.
(5) Assessment of clinical parameters through laboratory tests and medical evaluation.
(6) Thrombosis within the pump can compromise blood flow in three ways: (1) pre-pump thrombosis. (2) intra-pump thrombosis. (3) post-pump thrombosis at the level of out-flow graft and aortic anastomosis.

4.2. Risk Identification Study

It is standard practice in HAZOP to assemble a team of experts for the risk identification process within a facility or during specific processes [48]. However, this was not necessary in the present case, as the application example was based on the actions recommended by the medical team [25]. Table 2 consolidates information on the evaluated parameters, including the definition of guide words and deviations, with consideration given to the measurement resources. The information provided is based on the thrombosis adherence points in the device [25].

Table 2. Thrombosis adherence points, parameters, guide words, and HAZOP deviations.

Adherence Point	Parameter	Guide Word	Deviation
1	Heart failure (HF)	Yes	Symptoms of HF
1	Blood flow	Less	Acute decrease in blood flow
1	Electrical power consumption	Less	Acute decrease in energy consumption
2	Electrical power consumption	More	Increased energy consumption
2	Hemolysis	Yes	Symptoms of hemolysis
2	Third harmonic (acoustic analysis)	Yes	Presence of third harmonic
2	Heart failure (HF)	Yes	Symptoms of HF
2	Severe hemolysis	Yes	Symptoms of severe hemolysis
3	Blood flow	Less	Slow decrease in blood flow
3	Electrical energy consumption	Less	Slow decrease in electrical power consumption

An adverse activity was designated for each thrombosis adherence point in the device, facilitating the study of the undesirable events that arise from thrombosis adherence in three distinct regions, leading to the conception of an adverse process (AE1). Table 3 presents information on the adverse process (AE1), the associated adverse activities ((AE1.1), (AE1.2), and (AE1.3)), and their respective causes.

Table 3. Adverse process, adverse activities, and causes.

Adverse Process	Adverse Activity	Cause
Thrombosis in the device (AE1)	Pre-pump thrombosis (AE1.1)	Thrombosis in the inflow cannula
	Intra-pump thrombosis (AE1.2)	Thrombosis adhered to the rotor
	Post-pump thrombosis (AE1.3)	Thrombosis in the outflow cannula
		Thrombosis in the anastomosis (aorta and outflow cannula)

Once the complete description of the parameters evaluated in the adverse process AE1 was established, the risks involving the occurrence of pre-pump thrombosis were identified, and the recommended actions for each undesirable state were specified. Table 4 presents the risk identification results and the medical team's recommended actions for the adverse activity 'pre-pump thrombosis (AE1.1)'.

Table 4. HAZOP table for pre-pump thrombosis (AE1.1).

Guide Word	Deviation	Cause	Detection	Consequence	Recommended Actions
Yes	Symptoms of HF or persistent low flow	Pre-pump Thrombosis	Medical evaluation	Obstruction of inflow	Evaluate and correct hypovolemia, arrhythmia, or hypertension
Less	Acute decrease in blood flow		Analysis of controller log files		Thrombectomy, reassessment, and oral anticoagulation.
Less	Acute decrease in power consuption				

Table 5 presents the results of risk identification and the survey of recommended actions by the medical team for the adverse activity 'intra-pump thrombosis (AE1.2)'.

Table 5. HAZOP table for intra-pump thrombosis (AE1.2).

Guide Word	Deviation	Cause	Detection	Consequence	Recommended Actions
More	Increase power consumption	Intra-pump Thrombosis	Device alarms	Device malfunction	Thrombolysis, re-evaluation, and oral anticoagulation
More	Symptoms of hemolysis		Medical evaluation		
Yes	Presence of the third harmonic		Acoustic analysis		
Yes	Symptoms of HF		Medical evaluation		Pump exchange surgery
Yes	Symptoms of severe hemolysis				

Table 6 presents the risk identification results and the medical team's recommended actions for the adverse activity 'post-pump thrombosis (AE1.3)'.

Table 6. HAZOP table for post-pump thrombosis (AE1.3).

Guide Word	Deviation	Cause	Detection	Consequence	Recommended Actions
Yes	Symptoms of HF or persistent low flow	Post-pump Thrombosis	Medical evaluation	Obstruction of outflow blood flow	Evaluate and correct hypovolemia, arrhythmia, or hypertension
Less	Slow decrease in blood flow		Controller log analysis		Perform imaging to confirm diagnosis
Less	Slow decrease in blood flow		Controller log analysis		Perform imaging to confirm diagnosis
Yes	Outflow obstruction		Imaging diagnosis		Surgery for stent placement with carotid protection if obstruction confirmed
Yes	Anastomosis stenosis				Surgery for stent placement if stenosis in the anastomosis is confirmed

Medical evaluation is required for a conclusive diagnosis of all three adverse activities. The evaluated parameters are derived from indirect detection and are used in identifying deviations, among which the following are highlighted:

- Acoustic vibration analysis.
- Symptoms of hemolysis.
- Symptoms of HF.
- Echocardiographic diagnosis.

The following steps outline the modeling of the adverse process AE1, aimed at defining the diagnostic model for thrombosis in the device and the monitoring model for the corresponding mitigation activities involving the three scenarios previously presented.

4.3. Systematic Approach for SCVAD Modeling

The following sections provide guidelines for modeling the adverse process 'thrombosis in the fevice (AE1)'. Section 4.3.1 presents the development of the adverse process model 'thrombosis in the device (AE1)' to be encapsulated in an adverse event diagnostic module for the composition of the DMAD. Section 4.3.2 presents the development of the adverse process mitigation module AE1 for the composition of the DMAPM.

4.3.1. Adverse Process Modeling

Each PFS was transcribed into an interpreted PN based on the process modeling resources presented in Section 2.3, titled Formalisms for Process Modeling of Complex Systems. A legend in each PN references the elements used, namely, a discrete transition, discrete place, oriented arc, and enabling arc. The enabling arcs are used to represent data

flow with the external environment, and a table of inputs (transitions) and outputs (places) for the PN is provided in Appendix A to aid understanding. The transitions and places have been named as necessary to maintain a clean and clear design in the figures.

Figure 9 presents the digital adverse event diagnosis model (DMAD), which supports the specification of diagnostic modules for adverse processes associated with known adverse events. The 'adverse process diagnosis module AE1' presented in Figure 10 was developed through the HAZOP study for risk identification detailed in Section 4.2 and was further elaborated into three adverse activities:

- The PFS model 'pre-pump thrombosis AE1.1' is presented in Figure 11, with the corresponding PN in Figure 12.
- The PFS model 'intra-pump thrombosis AE1.2' is presented in Figure 13, with the corresponding PN in Figure 14.
- The PFS model 'post-pump thrombosis AE1.3' is presented in Figure 15, with the corresponding PN in Figure 16.

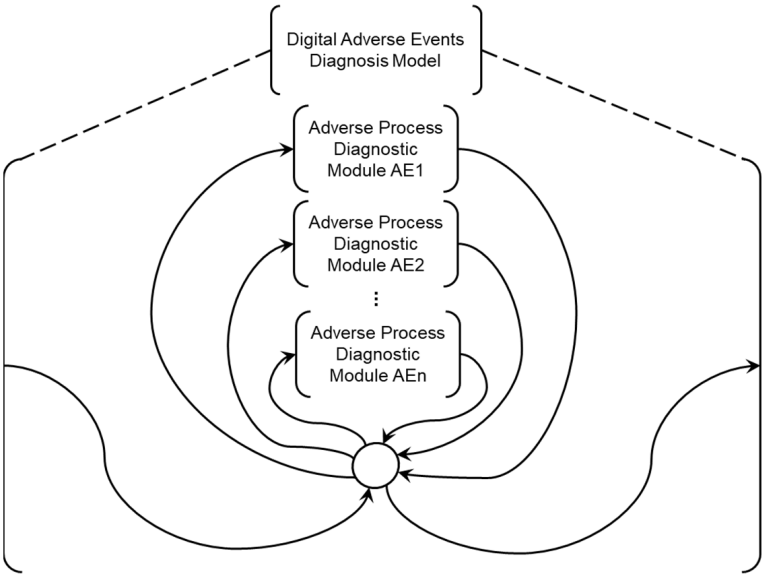

Figure 9. PFS and detailing of the digital model for adverse event diagnosis (DMAD).

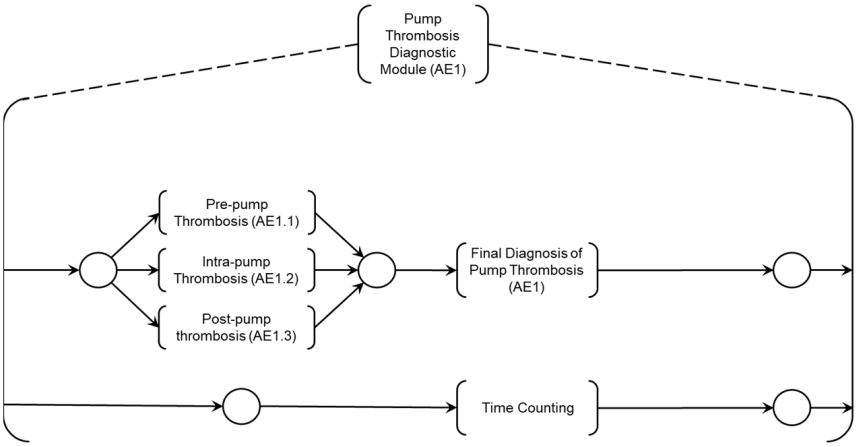

Figure 10. PFS and detailing of the diagnostic module for thrombosis in the device (AE1).

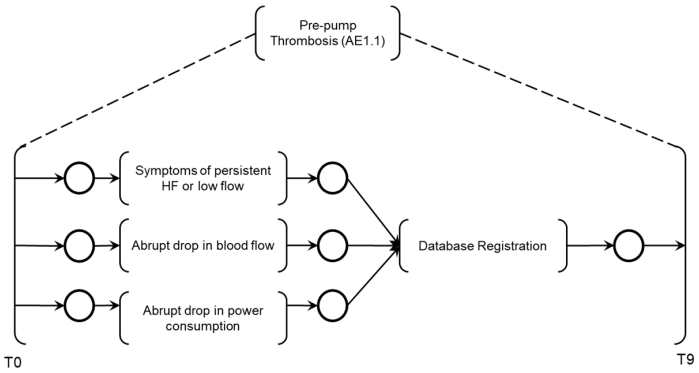

Figure 11. PFS and detailing of the adverse activity 'pre-pump thrombosis AE1.1'.

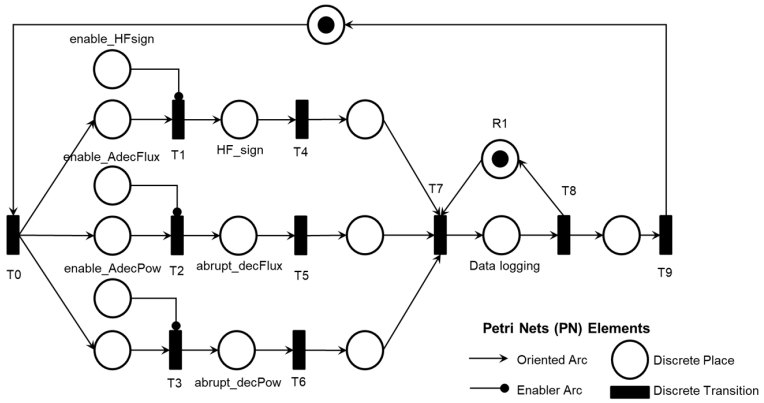

Figure 12. PN corresponding to the adverse activity 'pre-pump thrombosis AE1.1'.

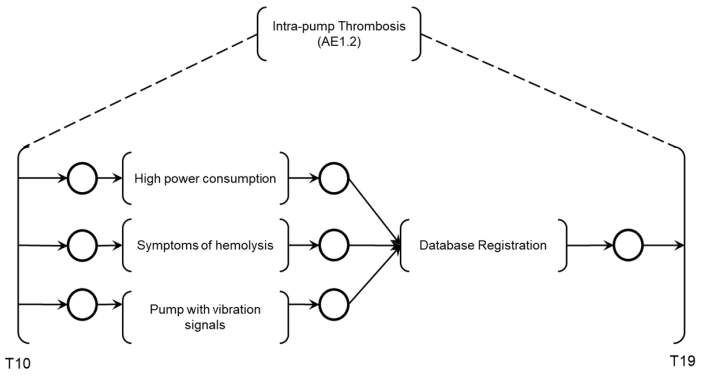

Figure 13. PFS and detailing of the adverse activity 'intra-pump thrombosis AE1.2'.

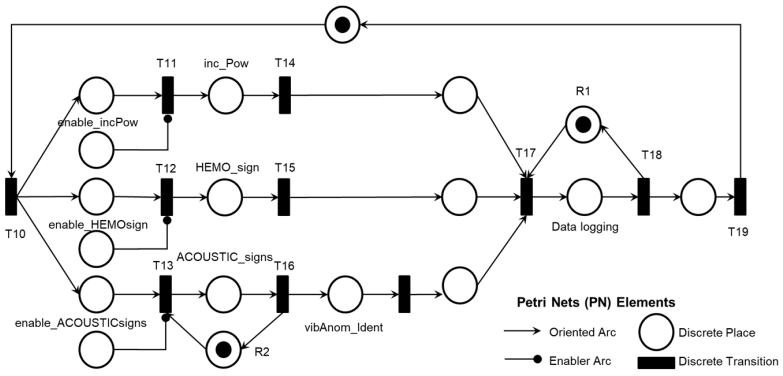

Figure 14. PN corresponding to the adverse activity 'intra-pump thrombosis AE1.2'.

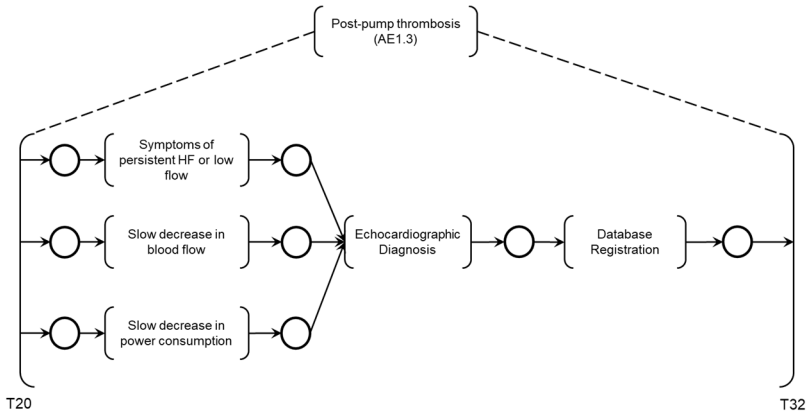

Figure 15. PFS and detailing of the adverse activity 'post-pump thrombosis AE1.3'.

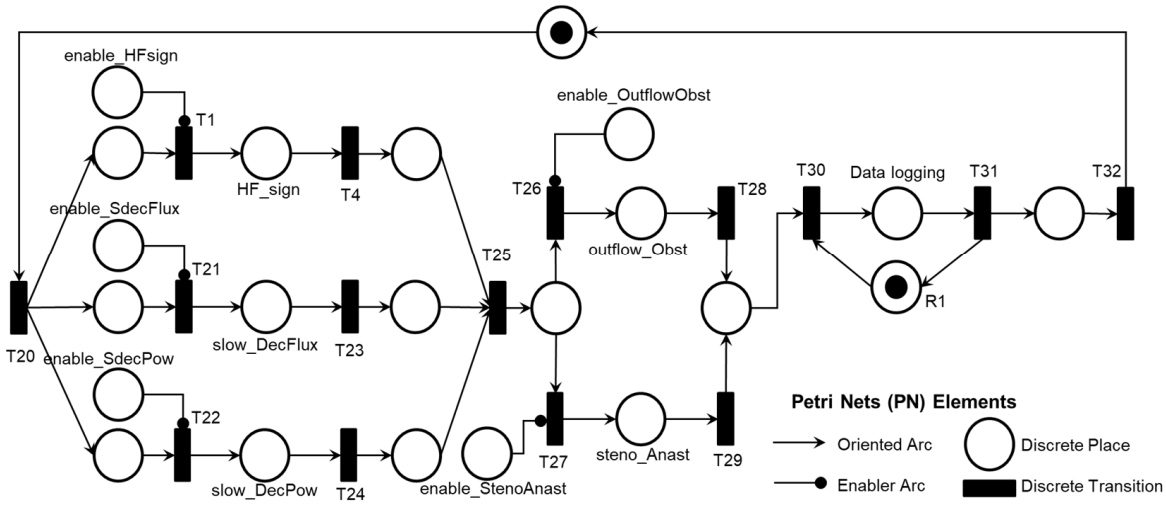

Figure 16. PN corresponding to the adverse activity 'post-pump thrombosis AE1.3'.

The mutually exclusive execution of activities AE1.1, AE1.2, or AE1.3 triggers the 'final diagnosis of pump thrombosis (AE1)', and the termination of the adverse process AE1 is determined by the timing executed by the 'time counting' activity.

As illustrated in Figure 11, the simultaneous execution of the activities 'symptoms of HF or persistent low flow', 'abrupt drop in blood flow', and 'abrupt drop in power consumption' enables the identification of pre-pump thrombosis and records this information through the execution of the 'database registration' activity.

Figure 12 illustrates the introduction of control elements and resources for sharing and representing data flow with the external environment.

As illustrated in Figure 13, the simultaneous execution of the activities 'high power consumption', 'symptoms of hemolysis', and 'pump with vibration signals' enables the identification of intra-pump thrombosis and records the information through the execution of the 'database registration' activity.

Figure 14 illustrates the introduction of control elements and resources for sharing and representing data flow with the external environment.

As illustrated in Figure 15, the simultaneous execution of the activities 'symptoms of HF or persistent low flow', 'slow decrease in blood flow', and 'slow decrease in power consumption' enables the diagnosis of the thrombosis location (anastomosis stenosis or obstruction at the outflow cannula) through the execution of the 'echocardiographic diagnosis' activity and subsequent recording of the post-pump thrombosis through the execution of the 'database registration' activity.

Figure 16 illustrates the introduction of control elements and resources for sharing and representing data flow with the external environment.

Finally, the diagnosis is carried out according to the logic described in the PFS model presented in Figure 17, considering the adverse activities 'pre-pump thrombosis AE1.1', 'intra-pump thrombosis AE1.2', or 'post-pump thrombosis AE1.3' detailed in the PN as illustrated in Figure 18. The conclusion of the adverse process AE1 is triggered by the execution of the activity 'final diagnosis of pump thrombosis (AE1)' concurrently with the execution of the 'time count' activity presented in Figure 19.

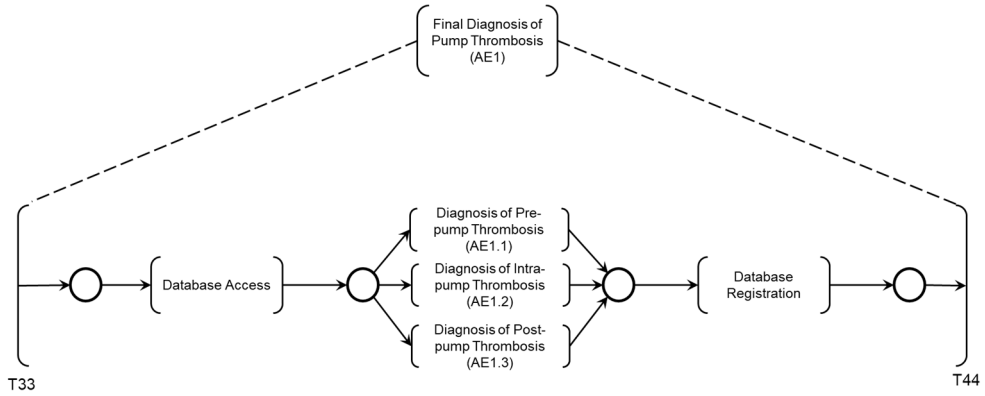

Figure 17. PFS and detailing of the activity 'final diagnosis of pump thrombosis (AE1)'.

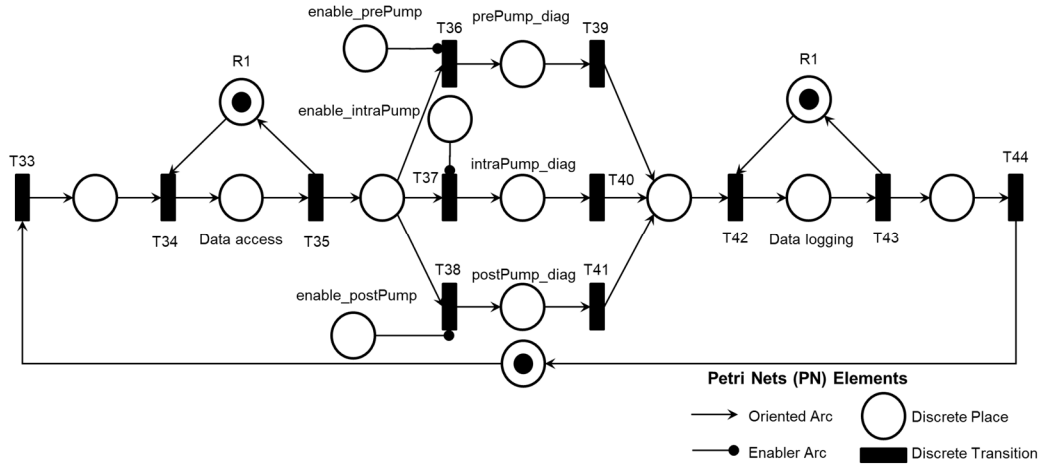

Figure 18. PN corresponds to the 'final diagnosis of pump thrombosis (AE1)' activity.

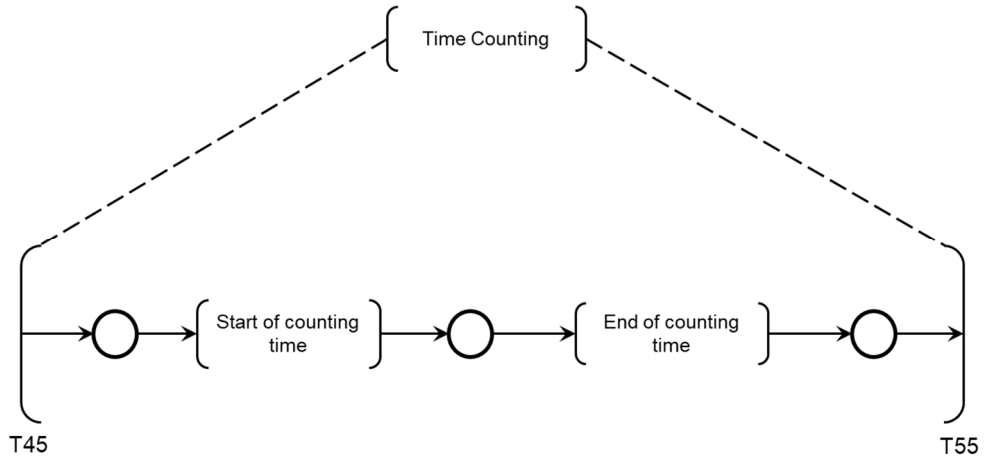

Figure 19. PFS and detailing of the activity 'time counting'.

As illustrated in Figure 17, following the execution of the 'database access' activity, information is collected to diagnose one of the adverse activities AE1.1, AE1.2, or AE1.3. Subsequently, the diagnosis of the adverse process AE1 is finalized and registered.

Figure 18 illustrates the introduction of control elements and resources for sharing and representing data flow with the external environment.

As shown in Figure 19, two sequential activities were specified for monitoring the maximum allowable time for patient care, namely, 'start of counting time' and 'end of counting time'.

The maximum patient care time is monitored using a countdown timer with watchdog logic. The medical team also interacts with the diagnostic modules, allowing the time count to be aborted by medical decisions if the adverse process deteriorates before the maximum allowed time is reached. The model in PFS for the 'end of time count' activity is shown in Figure 20, and the corresponding PN is shown in Figure 21.

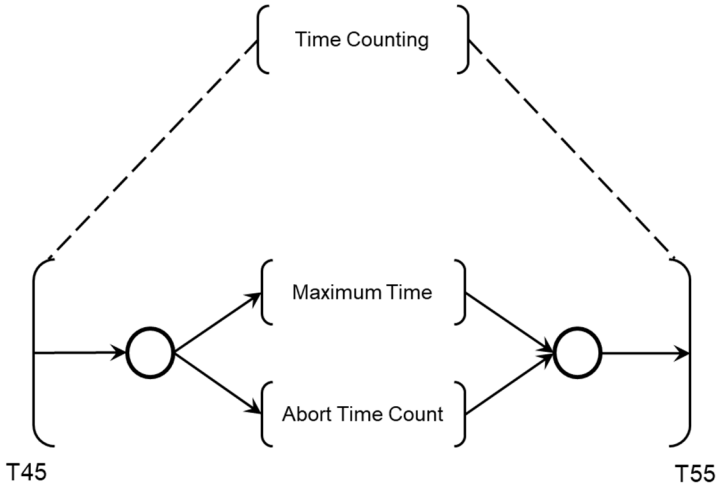

Figure 20. PFS and detailing of the activity 'end of counting time'.

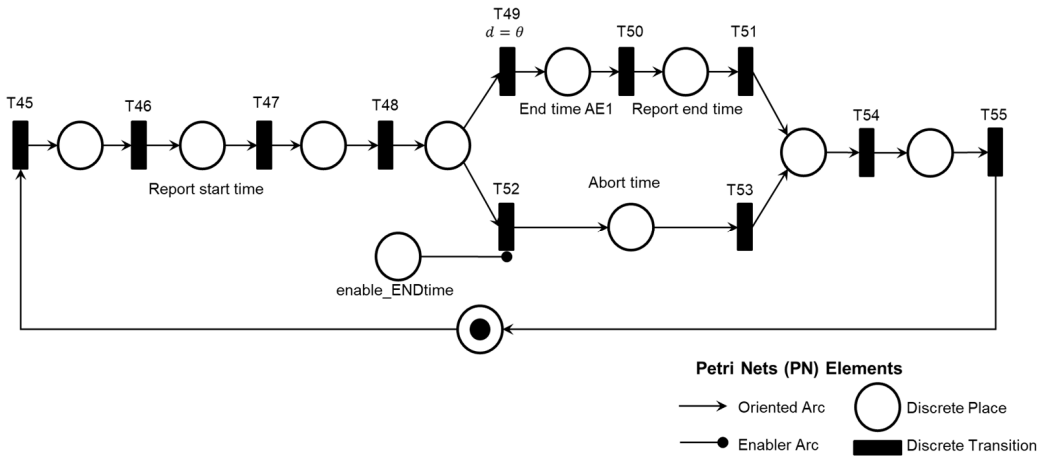

Figure 21. Corresponding PN for the 'time counting' activity.

As illustrated in Figure 20, two mutually exclusive activities determine the end of the time count, namely, 'maximum time', triggered by a countdown timer, and 'abort time Count', which can be triggered at any time by the medical team's command.

Figure 21 shows the introduction of control elements and resources for sharing and representing data flow with the external environment. Transition T49 is timed and functions as the watchdog for the adverse process.

4.3.2. Modeling of Intervention Protocols

Based on the previously presented diagnostic models, mitigation modules for adverse processes are specified, configuring intervention protocols defined by the medical team for the composition of the digital model for adverse process mitigation (DMAPM) shown in Figure 22. To address the patient's needs regarding critical adverse process AE1, the 'adverse process mitigation module (AE1)' was specified, as detailed in the PFS in Figure 23. The medical team specifies mitigation activities which will be detailed below.

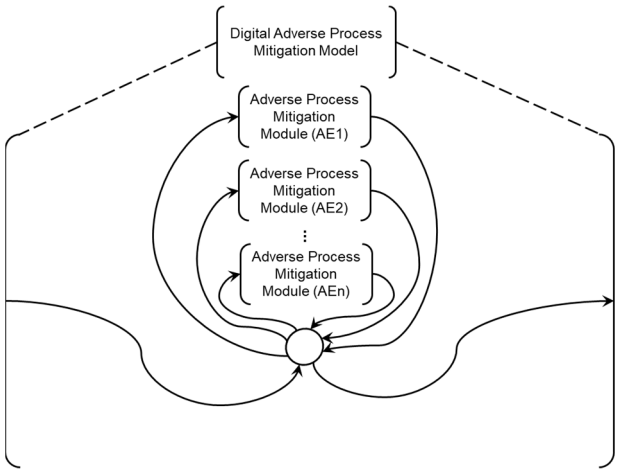

Figure 22. PFS and detailing of the digital model for adverse process mitigation (DMAPM).

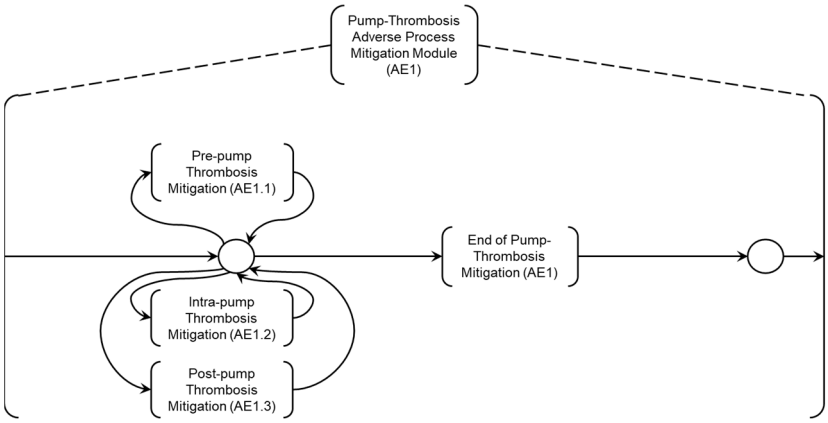

Figure 23. PFS and detailing of the thrombosis mitigation module for the device (AE1).

The activity 'pre-pump thrombosis mitigation AE1.1' is detailed in the PFS in Figure 24. When activated, the first mitigation activity that may be performed is 'thrombectomy', followed by patient supervision by the medical team based on monitoring the execution of required mitigation activities. Based on the recommended actions from the risk identification phase, activities that may be executed for the degeneration of adverse process AE1 include 'medical discharge' or 'pump exchange surgery'. Figure 25 illustrates the corresponding PN for the activity 'pre-pump thrombosis mitigation AE1.1', including control elements and resources for data flow sharing and representation with the external environment.

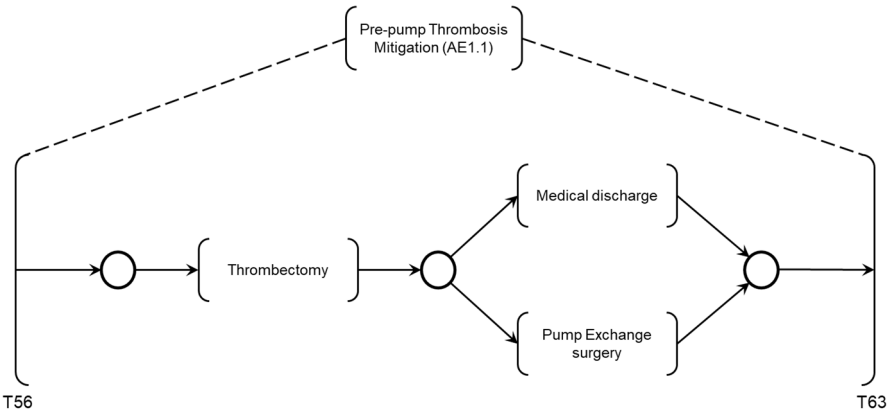

Figure 24. PFS and detailing of the activity 'pre-pump thrombosis mitigation AE1.1'.

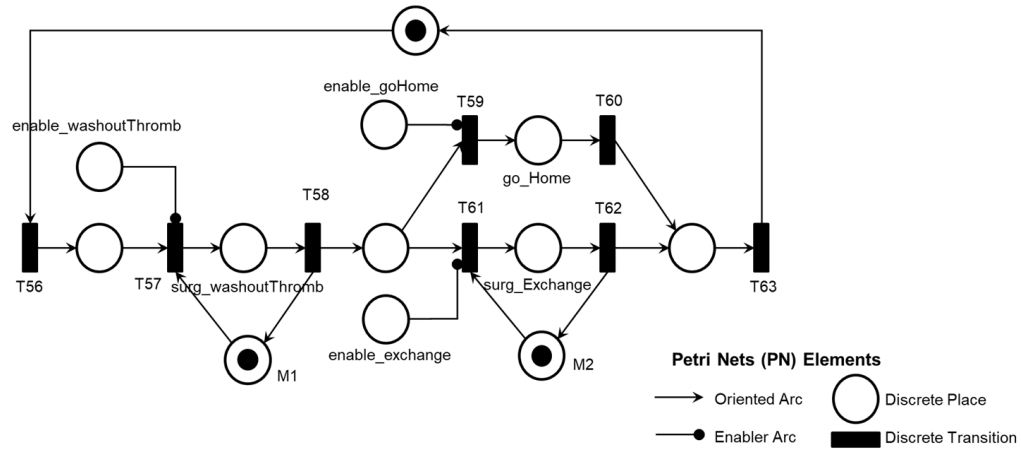

Figure 25. PN corresponding to the activity 'pre-pump thrombosis mitigation AE1.1'.

As illustrated in Figure 23, the activities 'pre-pump thrombosis mitigation AE1.1', 'intra-pump thrombosis mitigation AE1.2', and 'post-pump thrombosis mitigation AE1.3' are linked to the adverse process (AE1), which is subdivided into these adverse activities.

As shown in Figure 24, after executing the mitigation activity 'thrombectomy', two secondary mitigation activities may be enabled, namely, 'medical discharge', if the thrombosis is successfully removed, or 'pump exchange surgery', if thrombosis persists.

Figure 25 illustrates the introduction of control elements and resources for sharing and representing data flow with the external environment.

The activity 'intra-pump thrombosis mitigation AE1.2' is detailed in PFS in Figure 26. When enabled, the first mitigation activity that may be performed is 'thrombolysis', which degrades the adhered thrombus through clinical intervention. As mentioned, real-time information is provided for the medical team to monitor the execution of required mitigation activities. Based on the recommended actions from the risk identification phase, the activities that may be performed for the degeneration of adverse process AE1 include 'medical discharge' or 'pump exchange surgery'. Figure 27 illustrates the corresponding PN for the activity 'intra-pump thrombosis mitigation AE1.2', which includes control elements and resources for data flow sharing and representation with the external environment.

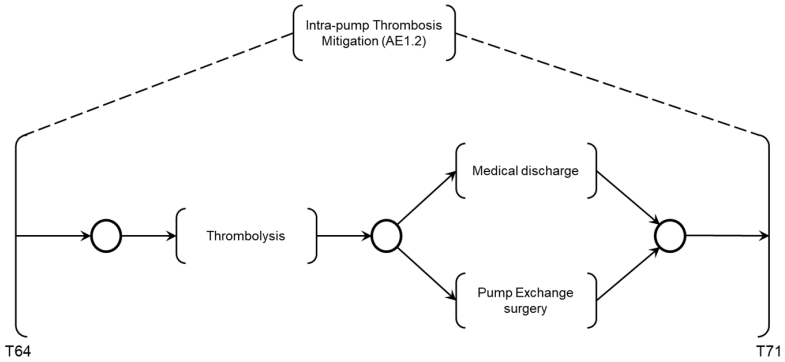

Figure 26. PFS and detailing of the activity 'intra-pump thrombosis mitigation AE1.2'.

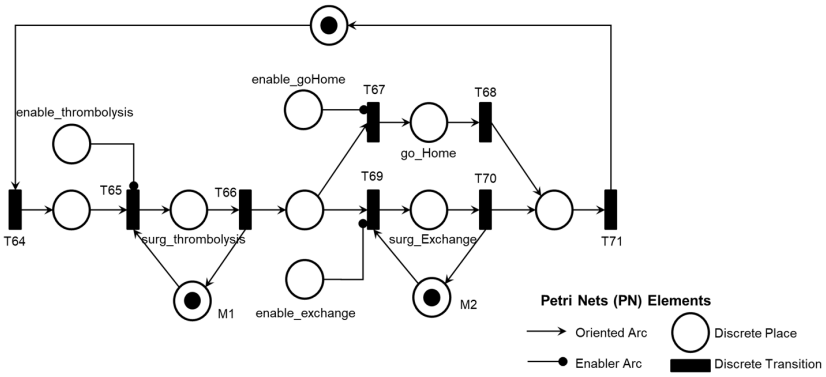

Figure 27. PN corresponding to the activity 'intra-pump thrombosis mitigation AE1.2'.

As shown in Figure 26, after executing the mitigation activity 'thrombolysis', two secondary mitigation activities may be enabled, namely, 'medical discharge' if the thrombus is successfully degraded or 'pump exchange surgery' if the thrombus persists.

Figure 27 illustrates the introduction of the control elements and resources for sharing and representing data flow with the external environment. Similarly to the previous activities, the 'post-pump thrombosis mitigation AE1.3' activity is detailed in PFS in Figure 28. When enabled, the first mitigation activity that may be performed is 'stent implant surgery' to restore adequate blood flow to the patient. As mentioned earlier, real-time information is provided to allow the medical team to monitor the execution of the required mitigation activities. The activities that may be executed for the degeneration of adverse process AE1, based on the recommended actions from the risk identification phase, include 'medical discharge', 'pump exchange surgery', or 'cannula position correction surgery', in the order defined by the supervising medical team. Figure 29 illustrates the corresponding PN for the activity 'post-pump thrombosis mitigation AE1.3', mentioning control elements and resources for data flow sharing and representation with the external environment.

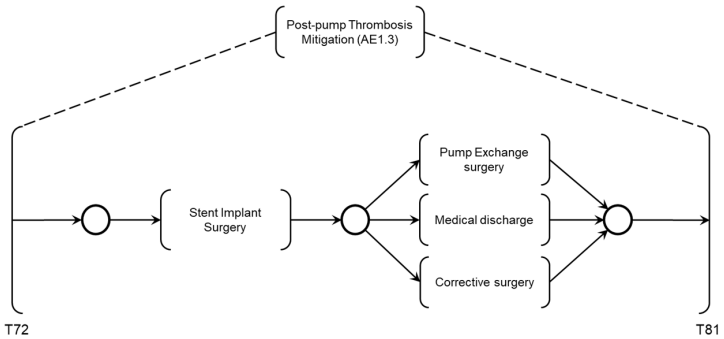

Figure 28. PFS and detailing of the activity 'post-pump thrombosis mitigation AE1.3'.

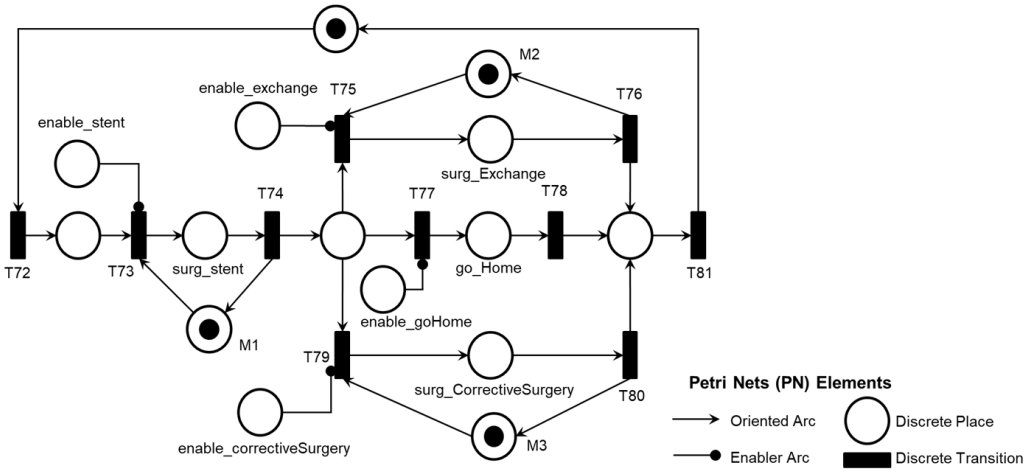

Figure 29. PN corresponding to the activity 'post-pump thrombosis mitigation AE1.3'.

As illustrated in Figure 28, after executing the mitigation activity 'stent implant surgery', three secondary mitigation activities may be enabled, namely, 'pump exchange surgery' if thrombosis persists, 'medical discharge' if adequate blood flow is restored, or 'corrective surgery' if repositioning of the outflow cannula is necessary.

Figure 29 illustrates the introduction of the control elements and resources for sharing and representing data flow with the external environment. The termination of the adverse process mitigation is enabled by the medical team's decision based on the execution of mitigation activities within the established time frame for adverse process AE1, as illustrated in the PFS in Figure 30 and detailed in the PN in Figure 31. Thus, the models are timed, and the medical team is informed to monitor the maximum time needed for the degeneration of the adverse process through the DMAD. The DMAPM communicates with the DMAD to allow the medical team to monitor and perform necessary mitigation activities to restore the patient's health state through the DMAPM.

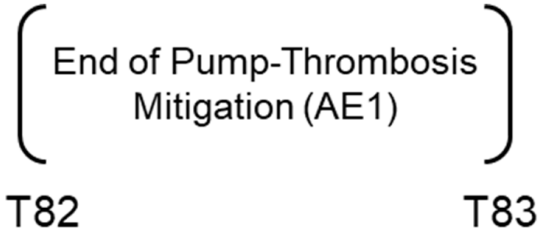

Figure 30. PFS of the activity 'end of pump thrombosis mitigation (AE1)'.

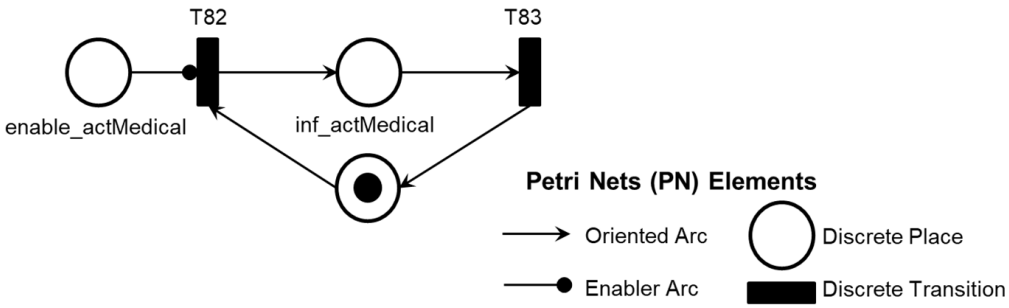

Figure 31. PN corresponding to the 'end of pump thrombosis mitigation (AE1)' activity.

Figure 31 illustrates the introduction of the control elements and resources for sharing and representing data flow with the external environment.

5. Discussion

This paper presents results based on an AE example to illustrate the method and demonstrate the steps for risk identification using HAZOP. The results presented represent models that consolidate the best practices in diagnosing and treating blood flow obstruction. Although the results are promising, they represent only one AE case; therefore, further studies should be conducted to complement the modules outlined for the SCVAD.

According to the IEC 31010 standard, another 31 techniques can be combined, and depending on the scenario, this is a factor that should be considered [50]. As previously mentioned, ISO 14971 provides guidance on the specification of techniques for the regulation of medical devices, particularly for VADs [49]. Therefore, a risk identification study can be conducted for each AE using techniques that meet the specific objectives and inherent characteristics of each AE.

Although the data collected from Scandroglio et al. [25] provided valuable information for obtaining important results in this work, this aspect can be improved, as the contribution of the medical team is fundamental and indispensable. They hold the specialized knowledge required to establish criteria that guide best practices for the diagnosis and treatment of AEs.

Another important point is that the method presents a formalism for obtaining logical models in PNs, which are validated through computational simulation and reflect the actions recommended by the experts. In this way, it can be ensured that the models used are a faithful and consistent representation of the actions recommended by the medical team, facilitating their application in a real-world context.

PNs also facilitate the transcription of these models into event-driven computable algorithms compatible with event-driven architecture (EDA). This allows interactions between the entities to be efficient and dynamic. In this way, the integration between the medical team and the other system entities can be established smoothly, ensuring that the necessary information for decision-making is always accessible and up to date.

In this context, APIs can be specified to allow the conversion of data from the physical environment, such as patient vital signs or monitoring sensor data, into a digital format. These APIs play a crucial role in making data available, which is essential for ensuring that medical decisions are based on up-to-date information.

Once made available, this data can be shared through an event broker using a publish–subscribe service. This mechanism facilitates instant communication between the entities involved in the process, enabling effective coordination in managing AEs, monitoring the patient's health, and executing mitigation actions when necessary.

6. Conclusions

With the application of the proposed method, it was possible to obtain timed models that allow for the supervision of the dynamic behavior of adverse processes initiated by the occurrence of AEs. The digitization of the adverse process promptly enables communication between the medical team and other entities, improving care for patients with implanted VADs. This way, it is possible to minimize patient harm and assess the risks associated with AEs.

In this context, a modular, event-oriented structure was established, allowing the medical team to monitor the dynamic evolution of unwanted states and supervise patient care processes, initiating interventions as needed.

The system's entities were organized to support horizontal and vertical integration. These are fundamental characteristics for implementing a system geared towards the Health 4.0 context [51,52], where collaborative interaction occurs between the VAD, the patient, and the supervising medical team.

With the presented results, new diagnostic and mitigation modules can be specified for the progression of the new adverse process. These are essential for health regeneration and significantly contribute to reducing the risk of death for patients with implanted VADs.

Therefore, the SCVAD provides a structure that allows the medical team to address the needs of patients, based on knowledge of adverse processes, as well as to specify new adverse processes identified within the community of patients with implanted VADs. This work aims to contribute to the development of supervision systems that align with new technologies present in the Industry 4.0 context [20] and to address the exclusive demands of an open system that fosters collaborative interaction among medical devices embedded in patients, the patients themselves, and medical teams, for the formulation of future intelligent systems geared towards Health 4.0 capable of meeting specific requirements for each patient.

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Abbreviations

The following abbreviations are used in this manuscript:

AE	Adverse event
AHA	American Heart Association
API	Application programming interfaces
BTR	Bridge to recovery
BTT	Bridge to transplant
CS	Critical system
DES	Discrete-event system
DMAD	Digital model for adverse event diagnosis
DMAPM	Digital model for adverse process mitigation
DT	Destination therapy
EDA	Event-driven architecture
FDA	Food and Drug Administration
HAZOP	Hazard and operability studies
HF	Heart failure
HM2	HeartMate 2
HM3	HeartMate 3
MDR	Medical device report
PFS	Production flow schema
PN	Petri nets
SCVAD	System for supervising critical adverse processes in patients with implanted ventricular assist devices
VAD	Ventricular assist device

Appendix A Inputs and Outputs of the PN Models

Table A1. Inputs and Outputs Associated with the Petri net models.

Inputs	Description	Outputs	Description
enable_ENDtime	Doctor enables decision to abort time count	HF_sign	Symptoms of heart failure (HF) or persistent low flow
enable_HFsign	Doctor enables identification of heart failure symptoms	abrupt_DecFlux	Indicates acute decrease in blood flow
enable_HEMOsign	Doctor enables identification of hemolysis symptoms	abrupt_DecPow	Indicates acute decrease in power consumption
enable_AdecFlux	Identification of acute decrease in blood flow	Data logging	Records occurrence in the database
enable_AdecPow	Identification of acute decrease in power consumption	Data access	Access to the database for reading
enable_incPow	Identification of increased power consumption	inc_Pow	Indicates increase in power consumption
enable_ACOUSTICsigns	Enables acoustic vibrational signal measurement	HEMO_sign	Indicates hemolysis symptoms
enable_SdecFlux	Identification of slow decrease in blood flow	ACOUSTIC_signs	Executes acoustic vibration analysis
enable_SdecPow	Identification of slow decrease in power consumption	vibAnom_ident	Indicates an anomaly in the acoustic vibration signal
enable_OutflowObst	Doctor enables identification of outflow cannula obstruction	slow_DecFlux	Indicates slow decrease in blood flow
enable_StenoAnast	Doctor enables identification of anastomosis stenosis	slow_DecPow	Indicates slow decrease in power consumption
enable_prePump	Enables diagnosis of pre-pump thrombus	outflow_Obst	Indicates obstruction in the outflow cannula
enable_intraPump	Enables diagnosis of intra-pump thrombus	steno_Anast	Indicates anastomosis stenosis
enable_postPump	Enables diagnosis of post-pump thrombus	prePump_diag	Indicates pre-pump thrombus diagnosis
enable_washoutThromb	Enables thrombus removal surgery	intraPump_diag	Indicates intra-pump thrombus diagnosis
enable_goHome	Enables medical discharge	postPump_diag	Indicates post-pump thrombus diagnosis
enable_exchange	Enables blood pump replacement surgery	Report start time	Indicates start time of the procedure
enable_thrombolysis	Enables thrombolysis procedure	Report end time	Indicates end time for expected care
enable_correctiveSurgery	Enables corrective cannula surgery	End time AE1	End of expected time for care
enable_actMedical	Doctor enables end of mitigation for adverse event (AE1)	Abort time	Indicates doctor's decision to abort time count
enable_stent	Enables stent implantation surgery	surg_washoutThromb	Performs thrombus removal surgery
		go_Home	Performs medical discharge procedures
		surg_Exchange	Performs blood pump replacement surgery

Table A1. *Cont.*

Inputs	Description	Outputs	Description
		surg_thrombolysis	Performs thrombolysis procedure
		surg_CorrectiveSurgery	Performs corrective cannula surgery
		inf_actMedical	Indicates end of mitigation for AE1
		surg_stent	Performs stent implantation surgery

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