Developing a decision-theoretic network for a congenital heart disease*

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Abstract

To support paediatric cardiologists in prognostic assessment and treatment planning, a decision-theoretic network for congenital heart disease is being constructed. The network is built in collaboration with a domain expert, using modelling methods commonly advocated in the literature. Although these methods prove to be useful in many cases, it was found that in some situations their applicability falls short. These situations and their associated problems are described. Techniques that have been developed to effectively deal with the problems are presented.

1 Introduction

Recent work in the fields of artificial intelligence and statistical decision theory has yielded the framework of decision-theoretic networks [15]. The framework combines explicit, declarative domain models known from artificial intelligence with normative theories of decision making under uncertainty. In contrast with the classical decision-theoretic and knowledge-based approaches employed in the past two decades to decision making under uncertainty, the framework of decision-theoretic networks couples expressiveness to mathematical correctness. The framework is therefore especially suited as a basis for decision-theoretic expert systems.

In building a decision-theoretic network, the origins of the framework are reflected [13]. As with any expert system, knowledge has to be acquired from domain experts, literature and databases. As such, the knowledge-acquisition process accords with the methodologies for knowledge engineering proposed in recent years (cf. [16]). These knowledge-engineering methods have to be supplemented with modelling techniques from decision analysis and statistics. However, due to the often large size and complex dependence structure of network models, application of the latter techniques is not straightforward in the context of decision-theoretic networks [4]. It is also not apparent how knowledge-engineering techniques and statistical methods must be combined. Although considerable effort is being spent on developing and

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maintaining network models (e.g., [1, 5, 6, 8, 9]), detailed methodologies for building decision-theoretic networks are currently lacking.

The Tetrade project aims at the development of methods and tools for knowledge acquisition for decision-theoretic network-based systems, tailored to the problem class of prognostic assessment and treatment planning in medicine. The field of *paediatric cardiology* was chosen as a test bed for gaining experience in building decision-theoretic networks. *Ventricular septal defect* is the most common disorder that the paediatric cardiologist is confronted with. It is therefore relatively well-understood, and comparatively large amounts of data on the disorder are available. As these circumstances render good opportunities for network construction and validation, ventricular septal defect was chosen as the first problem domain to be examined.

In this paper, we describe the building of the qualitative part of a network model for ventricular septal defects. In the next section, we briefly review the theory of decision-theoretic networks. Section 3 addresses the aspects of ventricular septal defects that are relevant for the examples given in Sect. 4, in which the development of the network model is discussed. We describe how methods commonly advocated for network construction may fail in some situations. Techniques that have been developed to effectively deal with these problems. The paper is rounded off with some conclusions and a description of our future work in Sect. 5.

2 Decision-Theoretic Networks

A *decision-theoretic network*, or *influence diagram*, is a concise representation of a decision problem. It comprises a qualitative and a quantitative part. The qualitative part of a decision-theoretic network encodes in a *directed acyclic graph* all variables that are relevant to the decision problem at hand. In the graph, three types of node are distinguished. A *decision node* represents viable decisions or actions that can be taken by the decision maker, a *probabilistic variable* represents an uncertain entity, the outcome of which cannot be selected by the decision maker, and the *value node* models the desirability of the various decisions and their consequences. The arcs in the digraph bear different meanings, depending on the types of their incident vertices. For example, the set of all arcs between probabilistic vertices captures the (conditional) independency relation between these variables; informally speaking, these arcs may be interpreted as directed 'influential' or 'causal' relationships between the linked variables. Associated with the qualitative part of the network is a quantitative part. This part consists of a numerical assessment of the strengths of the represented probabilistic relationships and of the desirabilities of the various decisions and their consequences. For the purpose of computing best decisions from a decision-theoretic network, several algorithms have been developed (e.g. [17]). *Belief networks* may be taken as decision-theoretic networks without decision and value nodes. In the design of a decision-theoretic network, a belief network can act as a convenient basis. In this paper, we restrict ourselves to the construction of belief networks.

Decision-theoretic networks may be abstracted to *qualitative networks* by replacing their numerical assessments with signs ('+', '−' or '?'), expressing qualitative influences and synergies [20]. Although qualitative networks are not as expressive as fully quantified networks, they bring several advantages. Qualitative networks may replace decision-theoretic networks where numerical assessments are either not available or not necessary for solving the decision problem at hand, or they may be used in addition to quantified networks for explaining

reasoning in qualitative terms [10]. Also, qualitative networks may serve as an intermediate representation in the knowledge-acquisition process [3]. In this paper, we address this last application of qualitative probabilistic networks.

3 The Problem Domain: Ventricular Septal Defects

A significant problem for the paediatric cardiologist in the management of patients with a cardiac anomaly is to decide if and when a patient has to be submitted to surgical treatment. In the management of these patients, there is always a trade-off between the benefits gained by waiting before surgical intervention in the hope that the patient's condition will improve, and the risks caused by the poor natural history of these disorders [14]. The number of factors involved in this decision-making process is large and their interplay is subtle. Therefore, it is extremely difficult for the clinician to determine which timing of medical and surgical treatment will be optimal for a given patient. In general terms, this problem may be characterised as planning under uncertainty with time constraints. Although the need for decision support in this problem domain is recognised by paediatric cardiologists, no system currently exists to support this decision-making process.

Ventricular septum defect (VSD) is a relatively well-understood disorder with many clinical features that are characteristic for congenital heart disease in general. It was therefore chosen as the first problem domain to be examined in the Tetrade project. VSD is a defect in the ventricular septum, the fibromuscular wall that separates the left and the right ventricle. An immediate consequence of this defect is blood flow ("shunt") from the left to the right ventricle due to ventricular pressure differences. The shunt size, *i.e.*, the amount of blood flowing through the defect, depends primarily on the size of the defect and the relation of pulmonary and systemic vascular resistances. During the foetal stage, the muscular pulmonary arteries are small in diameter with a thick smooth muscular wall, thus preventing massive shunting by their high resistance. Following birth, the arteries change to thin-walled structures with increased internal diameter. These changes are accompanied by a decline in pulmonary vascular resistance, resulting in an increased shunt size.

Left-to-right shunting causes oxygenous blood to be pumped into the lungs again. As a result, the pulmonary pressure will rise, and systemic cardiac output will decrease. The latter effect usually causes the patient to be pale and easily sweating. With large defects, the high pulmonary pressure (*pulmonary hypertension*) may lead to left heart failure, and also, in the long run, to right heart failure. Left heart failure is typically accompanied by shortness of breath, feeding problems, and a complex of symptoms that is usually termed 'failure to thrive'. Furthermore, abnormal breath sounds can be heard on auscultation (*pulmonary crepitations*). Signs of right heart failure are *cardiomegaly* (enlarged heart), *hepatomegaly* (enlarged liver), and *oedema*.

With small defects, the clinical course is favourable throughout infancy and childhood [11]. About 75 to 80% of the defects close spontaneously, with the majority closing in the first two years of life. Patients with moderate-sized defects may develop large left-to-right shunts and associated complications in infancy, but the majority of this group can be managed medically without surgical intervention. Patients with large defects are more difficult to manage, because of the risks of mortality in the first year of life due to heart failure and associated pulmonary infections. Elevated pulmonary vascular resistance may also develop as a response to continuous pulmonary overflow and hypertension [7]; this is termed *Eisenmenger's complex*.

It may result in severe, irreversible damage to the pulmonary arteries (*arteriopathy*). Early surgical intervention is therefore strongly recommended for these patients. The majority of patients with repair of uncomplicated VSD in infancy or early childhood have an excellent result with no clinical signs or symptoms and apparently normal long-term survival.

4 Building the Network Model

Building a decision-theoretic network for a domain of application involves various tasks. The first of these is to identify the *variables* that are of importance in the domain at hand, along with their possible values. Once the important variables have been identified, the construction of the qualitative part of the network can start: the second task is to identify the *probabilistic relationships* among the variables discerned and to express these relationships in an acyclic digraph. The last task in building a decision-theoretic network is to estimate the (conditional) probabilities that are required to constitute its quantitative part.

Here, we focus on the second task in the building of a network model: the construction of the qualitative part of the network, *i.e.*, the topology of the digraph. Formally, this task comprises identification of the independence relation of the joint probability distribution on the variables discerned. In practice, however, the digraph typically is constructed directly without explicitly identifying the independence relation. For most application domains, the qualitative part of a network model has to be *hand-crafted* with the help of one or more domain experts. For eliciting the topology of the digraph of the network, often the concept of *causality* is used as a heuristic guiding rule during the interview with a domain expert; typical questions asked are "What could cause this effect?", "What manifestations could this cause have?" [9]. The thus elicited causal relations among the variables discerned are easily expressed in graphical terms by taking the direction of causality for directing the arcs between related variables; this graphical representation can then be taken as a basis for feedback to the domain expert for further refinement. Building on the concept of causality has the advantage that domain experts are allowed to express their knowledge in either the *causal* or *diagnostic* direction. Since they are allowed to express their knowledge in a form they feel comfortable with, the experts' statements tend to be quite robust. This especially holds in medical domains, where the various factors involved in the clinical description of a disorder are often characterised in terms of cause-effect relations.

Yet, not every influential relationship among variables can be interpreted causally. If a non-causal influential relationship comes to the fore, a more elaborate analysis of the independences involved is required before it can be expressed in graphical terms. In the sequel, we discuss three situations where using causality as a principle modelling guideline may be confusing or even lead to incorrect results. For each of these situations, we provide a method to circumvent or solve the problem.

First, causality is not a well-understood concept and therefore may leave room for multiple interpretations. In particular, there may be substantial differences in the amount of time it takes for 'causes' to render their 'effects'. Sometimes the relations described by directed graph found in medical textbooks are better understood in terms of state transitions over time than in terms of causality. This was one of the reasons that we decided to make a separate description of the clinical course of VSD in terms of major pathophysiological development stages. This description complements the static description provided by the network model; a full account is given in Subsect. 4.1. A second situation in which causality may hamper instead

of help the construction of the digraph is the presence of feedback loops. To avoid directed cycles in the topology of the digraph, alternative modelling techniques are then required. In Subsect. 4.2, we discuss two example feedback loops in the VSD domain, and the way we decided to model them. Finally, it is not uncommon to find many qualitative abstractions in the vocabulary of a clinician. Such abstractions cannot be understood in terms of cause-effect relations, and therefore have to dealt with differently. The modelling of abstractions is discussed in Subsect. 4.3.

4.1 Modelling Development Stages of a Disorder

One of the problems we encountered during model building was the fact that there are several stages in the pathophysiological development of a VSD, and each stage has its own characteristics. Although it was possible to construct a single, static model that accounted for each of the stages and its characteristics, the resulting model did not seem to suit the clinician's intuition very well. For instance, this model (to which we will refer as the *general network model*) includes a variable SHUNT, taking a value from the domain {*no_shunting*, *small_left-to-right_shunt*, *large_left-to-right_shunt*, *right-to-left_shunt*}. Among the successors in the digraph of this variable are included both typical signs of left-to-right shunting, such as paleness and sweating, as typical signs of right-to-left shunting, such as cyanosis. Simultaneous occurrence of these signs, however, is excluded. As the domain expert pointed out, it is therefore not very natural to see these signs co-occurring in a single network model.

Our solution to this problem consisted of the following steps. First, the pathophysiological stages of the disease development were identified. Then, we explored which reductions to the general network model were possible in each stage. The models resulting from applying these reductions are called *stage models*. They are reduced versions of the general model, and contain only the parts that are relevant for the associated pathophysiological development stage. Reductions of the model consist of (possibly partial) value assignments to variables and removing variables and relations where possible.

The stages in the pathophysiological development of a VSD were distinguished by the domain expert. First, there is an initial stage (six to thirteen weeks after birth) during which the pulmonary vascular resistance decreases and the left-to-right shunt increases. In the second stage the left-to-right shunt has reached its maximum, causing heart failure with its associated signs. Subsequently, in the third stage, (a) either the defect size gradually decreases or (b) the Eisenmenger's complex may follow. In both cases left-to-right shunting will diminish, rendering a significant improvement in the condition of the patient. However, whereas decreasing defect size will lead to defect closure and vanishing clinical signs (fourth stage, a), increased pulmonary vascular resistance due to Eisenmenger's complex will eventually cause shunt reversal and cyanosis (fourth stage, b).

Central to model reduction was the variable SHUNT. Recall that right-to-left shunting is excluded in the first three stages of development. We can therefore remove the value *right-to-left_shunt* from the variable's domain in the associated stage models. Consequently, a number of variables representing characteristic effects of right-to-left shunting (e.g., CYANOSIS) can be removed from the stage models. On the other hand, left-to-right shunting cannot occur in the fourth stage. So, the values *small_left-to-right_shunt* and *large_left-to-right_shunt* can be excluded from the SHUNT domain in the stage model for stage IV. In this case, the variables representing characteristic effects of left-to-right shunting (e.g. HEART FAILURE and PULMONARY FLOW-HYPERTENSION) can be removed.

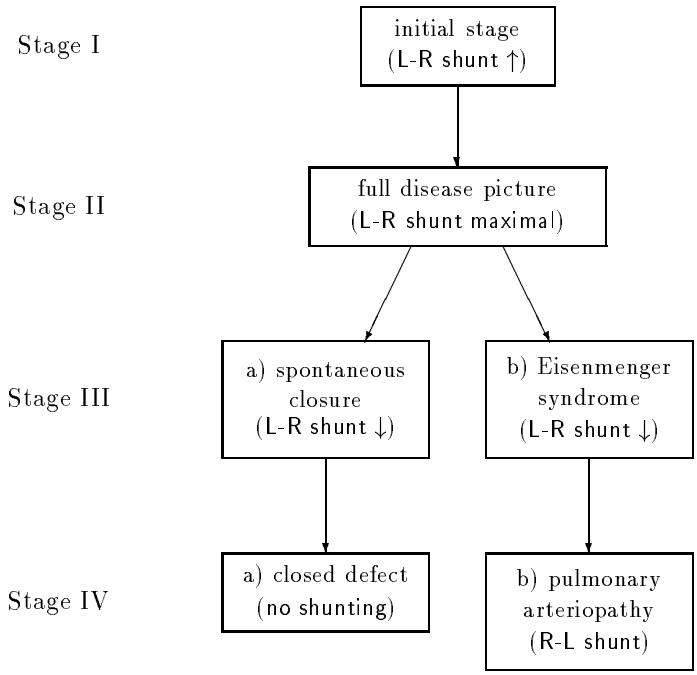

Figure 1: Stages in the pathophysiological development of a VSD.

Node removal is valid in these cases because some of the relations between the variable SHUNT and its successors are not probabilistic but *deterministic* in nature. Deterministic relations can often be detected in the vocabulary and reasoning of the clinician. In the present example, it was detected that the domain expert often equated 'right-to-left shunting' and 'cyanosis' in his explanations. Detecting deterministic relations is useful in several respects: it reduces the number of probabilities that have to be assessed, and can be used to infer strong conditional independency statements that facilitate efficient computations [19].

4.2 Coping With Feedback Loops

The main physiological component in the domain of congenital heart disease is a closed-loop haemodynamic system. It is not very surprising, then, that one of the problems we were confronted with during model development was the occurrence of *feedback loops*. In the case of a VSD, the size of the left-to-right shunt depends on the interventricular pressure gradient, which in turn depends on the relative pulmonary pressure (compared to systemic pressure). On the other hand, the relative pulmonary pressure is increased by the shunting of blood through the defect. When we try to model these dependences in causal fashion, a (directed) cycle occurs in the network (see Fig. 2a).

Another example feedback process is Eisenmenger's complex. Continued left-to-right shunting through the VSD will increase the pulmonary arterial pressure. In time, this results in damage to the pulmonary arterioles, and increasing pulmonary vascular resistance. Although the pulmonary pressure will remain high, the pulmonary blood volume (*i.e.*, the shunt size) will decrease. This is depicted in Fig. 2b.

We note that a cyclic digraph representing a feedback process can be viewed as a compact

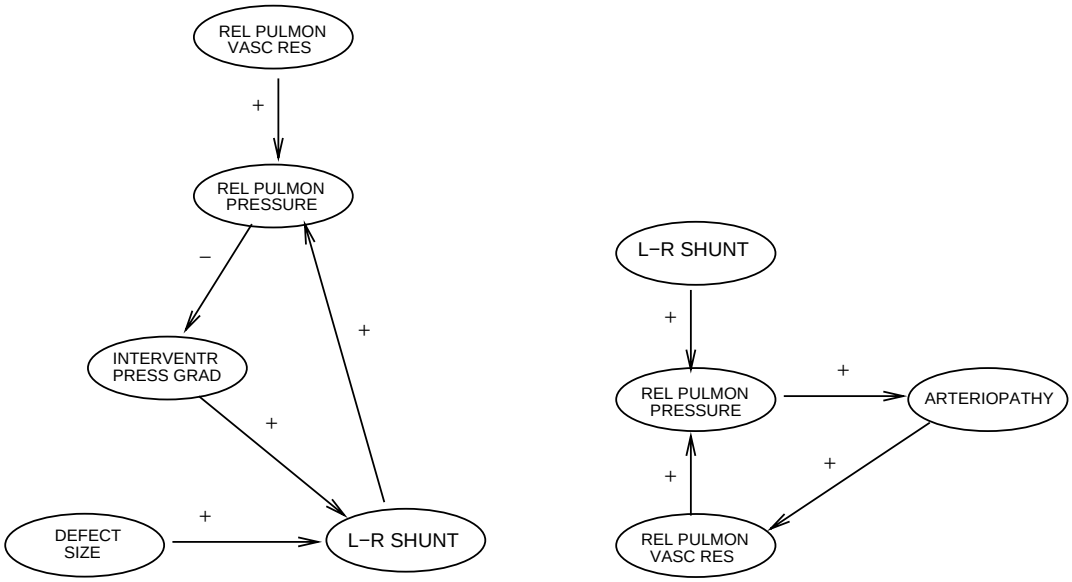

Figure 2: (a) haemodynamic feedback loop, and (b) Eisenmenger's complex.

representation of an infinite acyclic digraph containing each variable indexed by time [18]. A possible solution to the problem of directed cycles is therefore to reject the compact representation and to explicitly model the feedback process in a *dynamic network model* [2]. Dynamic network models extend the belief-network formalism by allowing temporal reasoning over a series of (structurally identical) static networks ("slices") indexed by time.

Although dynamic network models provide an elegant and mathematically sound way to represent feedback processes, their usefulness in practical circumstances is limited. Not only the size of the network model and computational complexity increase drastically, dynamic representation of the feedback process is also very fine-grained, and a regression model of the feedback process is needed. Therefore, we think that dynamic network models only should be used when the time spanned by the feedback process is large and multiple observations on the variables involved may be performed within that time span. This applies to the feedback process due to Eisenmenger's complex: this process may take several years, and usually many observations on the clinical state of patient are made during this period. The dynamic part of the network model for Eisenmenger's complex is shown in Fig. 3b (see below for an explanation of the variable PRESSURE RATIOS).

For short-term feedback processes, a solution within the static domain model is favourable. Then, an alternative representation without directed cycle has to be found, for which various options exist. These include adding and removing arcs, reversing one or more arcs, adding one or more variables to the digraph, and clustering multiple variables in a single network node. We do not believe there is a single, best option; the solution that is chosen should, however, yield a satisfactory model and be supported by domain-specific arguments. An example of solution of 'cutting' cycles by adding and removing arcs supported by domain-

specific arguments can be found in [12]. We have chosen to cluster the variables RELATIVE PULMONARY PRESSURE and INTERVENTRICULAR PRESSURE GRADIENT into one super node PRESSURE RATIOS. The argument is that in under normal circumstances, the values of the two aforementioned variables are equal; the clinician considers both variables to be known with certainty once either of both has been observed. Subsequently, a topology for the network containing the super node was designed in collaboration with the domain expert. The relevant part of the resulting network is shown in Fig. 3a.

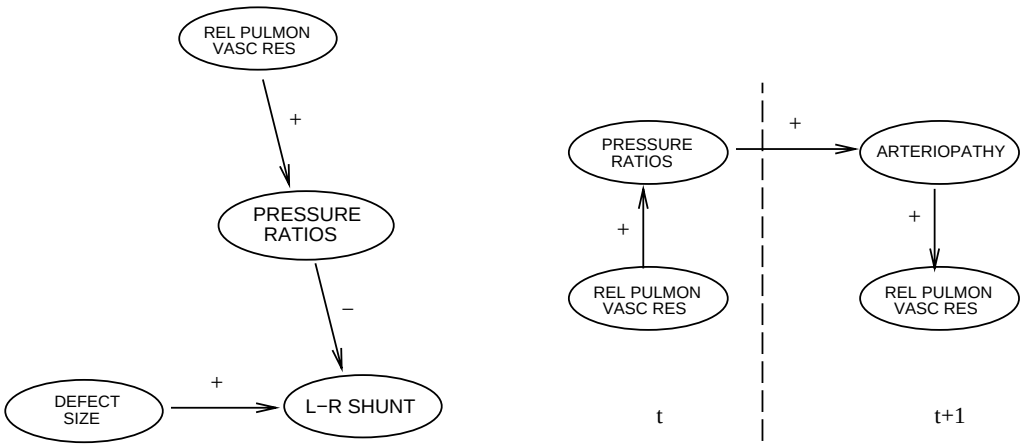

Figure 3: Solutions: (a) using a super node, and (b) dynamic network model.

4.3 Modelling Qualitative Abstractions

In many medical domains, the vocabulary that is used by clinicians contains qualitative abstractions of biochemical and physiological states or processes involved. Typically, a specific term is introduced to indicate that some quantity has reached some (critical) value, or that a typical combination of values is at stake. For instance, in the domain of cardiac anomalies, when the oxygen saturation of the systemic blood drops below 92%, this is classified as *cyanosis*. Similarly, when the systolic pulmonary pressure exceeds 1/4 of the systolic systemic pressure due to large left-to-right shunting, one speaks of *pulmonary flow-hypertension* (see Fig. 4.3).

It is useful to recognise such abstractions during the model building for several reasons. First, there is usually a "hard" condition involved in the classification step; We have indicated this in Fig. 4.3 by the label 'c: $>$ 1/4' on the arc between RELATIVE PULMONARY PRESSURE and PULMONARY FLOW-HYPERTENSION. As was noted in Subsect. 4.1, recognition of such deterministic relations reduces the number of probabilities to be assessed. Second, if an abstraction variable has successors in the digraph, this will usually indicate an undesired loss of precision. It will be favourable to re-evaluate the relation between these nodes and the predecessors of the abstraction variable; In many circumstances, a direct, influential relation can then be found. Returning to the aformentioned example, our domain expert initially

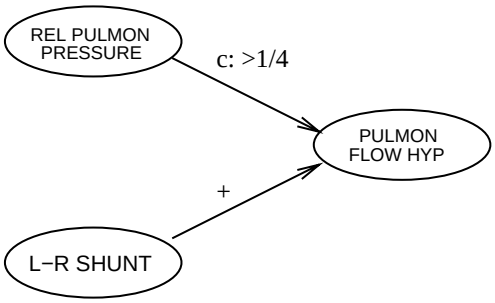

Figure 4: Abstraction variable.

stated that pulmonary flow-hypertension causes arteriopathy in the long run. While this is not untrue, it is more precise to state that continuous elevated pulmonary vascular pressure causes arteriopathy. As the pulmonary vascular pressure is modelled in quantitative terms, modelling the latter relation instead of the former yields more precision. We remark that the introduction of an abstraction variable has no effect on the complexity of the network model if the classification variable has no successors in the digraph. This is due to the fact that the variable itself will not be instantiated. Therefore, no dependencies between its predecessors in the graph are introduced.

Figure 5 shows the network model for VSD in stage III. We have made a distinction between primary and secondary determinants of the patient's clinical state, and variables whose values only result from this state, but do not have effect on others. In the case of VSD, the clinical state of the patient depends primarily on the size of the defect and the relative pulmonary vascular resistance. These variables are grouped by the dashed box with label A in the figure; They determine the state of variables like the relative pulmonary pressure, ventricular pressure gradient, direction and size of the shunt and the degree of heart failure. Dashed box B contains these secondary determinants. These variables in turn affect the state of many observable variables representing signs and symptoms. Finally, we have distinguished to variables that represent critical developments in the clinical state of the disorder. These are spontaneous closure of the defect, and Eisenmenger's complex; They are contained in dashed boxes with label C.

5 Conclusions and Future Work

The framework of decision-theoretic networks is becoming increasingly popular as a basis for medical decision-theoretic expert systems. The framework has proven its usefulness in a number of real-world applications. However, detailed methodologies for building decision-theoretic networks are still lacking.

In this paper, we have described the manual construction of network model for ventricular septal defect with the help of a paediatric cardiologist. We followed the often advocated heuristic of using 'causality' as a guideline in the modelling process. Although this heuristic proved to be useful in large part, it was found that in some situations its applicability falls short, or even may hamper efficient model construction. These include the situation that several stages of development are discerned in the clinical state of the patient, that feedback

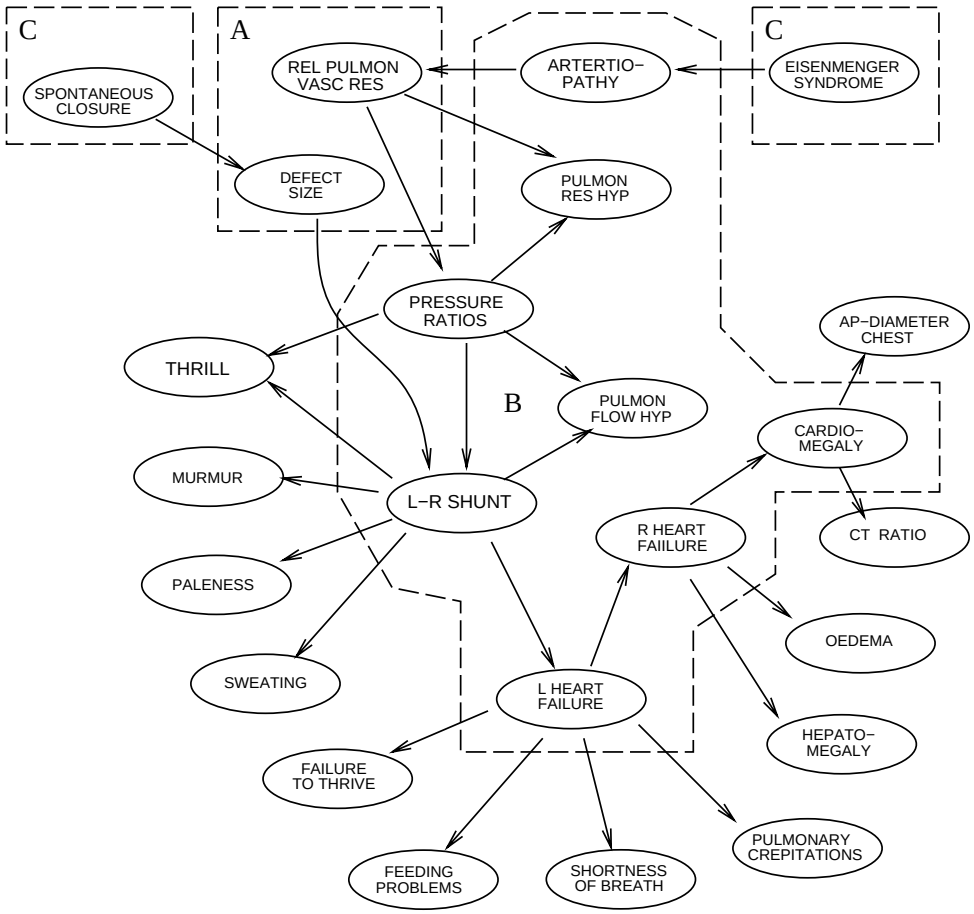

Figure 5: VSD model for stage III.

processes may exist in the domain, and that qualitative abstractions are used. To deal with each of these situations, specific techniques have been developed.

We have described a simplified version of the VSD model that will be used as a basis for a decision-theoretic expert system. We are currently implementing the model, which counts up to 38 nodes and 52 arcs, as a qualitative probabilistic network. The resulting preliminary system will be used as feedback to the domain expert for possible refinement. Subsequently, the numerical probabilities forming the quantitative part of the network model will be assessed. For this task, the framework described in [3] will be used to combine numerical information from various sources. Finally, the model will be embedded in a decision-support architecture.

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