A Markov Decision Process Model to Guide Treatment of Abdominal Aortic Aneurysms

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Abstract—An abdominal aortic aneurysm (AAA) is an enlargement of the abdominal aorta which, if left untreated, can progressively widen and may rupture with fatal consequences. In this paper, we determine an optimal treatment policy using Markov decision process modeling. The policy is optimal with respect to the number of quality adjusted life-years (QALYs) that are expected to be accumulated during the remaining life of a patient. The new policy takes into account factors that are ignored by the current clinical policy (e.g., the life-expectancy and the age-dependent surgical mortality). The resulting optimal policy is structurally different from the current policy. In particular, the policy suggests that young patients with small aneurysms should undergo surgery. The robustness of the policy structure is demonstrated using simulations. A gain in the number of expected QALYs is shown, which indicates a possibility of improved care for patients with AAAs.

Index Terms—Abdominal aortic aneurysm (AAA), biosystems, decision making, Markov decision process (MDP), public health-care, treatment policy

I. INTRODUCTION

For any kind of surgical intervention, the risks involved in the operation must be weighed against the potential benefits. In this paper, we focus on the question of when an abdominal aortic aneurysm (AAA) should be treated. AAAs are enlargements of the aorta that in general are asymptomatic. They, however, pose a threat of fatal rupture. Surgery aims to prevent this rupture, and thereby maximize the remaining life expectancy of the patient. The procedure is major surgery and can itself lead to death.

Each year during the lifetime of a patient with an AAA, the surgeon is faced with the question “should surgery be performed?” Since the diameter of an aneurysm is closely related to its rupture risk, the current clinical guidelines for treatment of AAAs state that surgery is recommended if the maximal aortic diameter exceeds 55 mm [2]. This treatment policy is not patient-specific, in the sense that it does not take into account factors such as the life-expectancy or the expected surgical mortality of the patient.

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The question that the surgeon faces can be seen as a problem of sequential decision making under uncertainty. Such problems have previously been studied in the control theory and operations research communities under the name Markov decision processes (MDPs), see, e.g., [3] or [4].

In this paper, the course of events and decisions resulting in the (potential) rupture or treatment of an AAA is modeled using an MDP. The resulting policy can guide the choice of treatment on a per patient basis: Given the diameter of the AAA and the age of the patient, an optimal choice of treatment can be read from a table that is presented in Section IV. The table is the result of optimizing the expected number of quality adjusted life-years (QALYs) over the patient’s remaining lifetime, where age dependent surgical and background mortalities have been taken into account. The robustness of the policy, with respect to the uncertainty in the model parameters, is assessed through simulations.

The main contributions of this paper are two-fold:

• Firstly, we demonstrate how the treatment of AAA can be modeled using the MDP framework.
• Secondly, and the main conclusion, is that the policy currently employed in clinical practice does not have an optimal structure.

The rest of this paper is organized as follows. Section II presents a brief overview of AAAs and the QALY measure. It then proceeds with a general outline and the notation of MDPs. In Section III it is explained how the problem allows an MDP formulation, as well as a discussion of the numerical parameters used in the model. Section IV presents the computed optimal policy and asserts the robustness. Section V concludes the paper with a discussion of related work and indications for further extensions.

II. BACKGROUND AND PRELIMINARIES

A. Abdominal aortic aneurysms

An aneurysm is a balloon-like dilatation of an artery [2]. They can occur in all arteries, but are most common in the infra-renal aorta and are there referred to as AAAs. Figure 1 depicts computerized tomography (CT) angiograms of a normal non-aneurysmatic aorta and an AAA.

The disease is characterized by loss of structural integrity in the wall of the abdominal aorta [5]. This, in most cases, leads to a progressive widening of the aneurysmal dilatation, that can potentially rupture [5]. The rupture of an AAA leads to massive hemorrhage and is a medical emergency. It is fatal in
Two different techniques exist for the treatment: open surgical repair (OSR) and endovascular aortic repair (EVAR). In OSR the diseased part of the aorta is replaced with a synthetic graft. After the surgery, the patient does not require any special follow-up, and is in essence cured from the disease [5]. In the EVAR technique, a stent-graft is placed inside the AAA through the arteries of the legs. This procedure requires that the patient is regularly followed up post-operatively to monitor the development of complications [5]. There is no consensus on which technique is superior. Several studies have shown similar long-term mortality with both techniques, see [5] and [2]. Instead, the choice depends on the anatomy of the aneurysm, the health status of the patient, the experience of the surgeon and patient preference [2].

The risk of rupture of an AAA is closely related to the aneurysm diameter. Guidelines state that AAAs should be operated if the diameter of the aneurysm exceeds 55 mm [2]. This exact threshold of 55 mm was chosen based on expert consensus (see [7] and [8]): All surgeons would operate patients who had an aneurysm that exceeded 60 mm, but there was no clear consensus on the policy for smaller AAAs. This criterion has by randomized controlled trials been shown to be superior to a strategy where also small AAAs are operated [2].

The current policy, however, is not perfect. It was recently shown that a significant proportion of AAA rupture before reaching the operative diameter threshold of 55 mm [9]. It is also known that some AAAs remain intact even after reaching a considerable diameter (>80 mm), see [9] and [10].

There are patient-specific exceptions to the 55 mm policy. It is generally recommended that women, who have larger risk of rupture, are operated when they reach 52 mm instead of 55 mm [2]. Also, most surgeons refrain from intervention if the patient suffers from serious co-morbidities (e.g. terminal cancer or heart disease) as this may increase the operative risk, patient suffering or not be of any conceivable benefit to the patient. But, no rigorous method exists for supporting the construction of these exceptions.

For an extensive review on the subject of AAAs, see [5].

B. Quality adjusted life-years

For a policy to be optimal it must specified with respect to what measure. A quality adjusted life-year (QALY) is a measure that describes the quality of life. Living one year at perfect health is equivalent to one QALY, and conversely one year dead is equivalent to zero QALYs. QALYs are used to provide more nuanced descriptions of health states compared to simply counting life-years, and are therefore commonly used in health-economic and outcomes research [11].

C. Markov decision processes

A widely used framework to model autonomous discrete-time stochastic systems is the Markov chain model (see, e.g., [12]). In this model, the system is assumed to transition randomly between a countable number of possible states. An MDP is an extension of this model in which the evolution of the system can be influenced by the choice of an action at each time instant. Solving an MDP means finding an optimal action to take, with respect to some reward function, at each possible state of the system and at each point in time. Such a mapping, not necessarily optimal, is called a policy.

It has previously been demonstrated that the time-evolution of an AAA (including growth and rupture risks) can be modeled using a Markov chain, see [13] and [14]. A natural extension, and the topic of the present work, is to formulate the decision making problem for AAAs – whether to take an action (i.e., perform surgery) or not – as an MDP.

Formally, we let the state of the Markov chain at time k be \( x_k \) which resides in the state-space \( \mathcal{X} \) with \( X \) elements. The transition probabilities are given by

\[
p_{ij}(u, k) = \Pr[x_{k+1} = j|x_k = i, u_k = u],
\]

where \( i, j \in \mathcal{X} \) are states, \( u \in \mathcal{U} \) is an action and \( \mathcal{U} \) is a (finite) set of available actions. The interpretation is that the transition probability \( p_{ij}(u, k) \) denotes the probability that the system will be in state \( j \) at the next time instant, given that it currently (time \( k \)) is in state \( i \) and that the action \( u \) has been chosen. The set \( \mathcal{U} \) can in general be time and/or state dependent, but it will be sufficient for our purposes to only consider a constant set.

The aim of the MDP is to find actions that maximize the expectation of some accumulative reward. We let the reward acquired at each time instant be a mapping \( r : \mathcal{X} \times \mathcal{U} \times \{M, M+1, \ldots, N\} \to \mathbb{R} \), where \( N-M \) is the length of the time horizon over which we consider the sequential decision problem. We interpret \( r(i, u, k) \) as the reward acquired by applying action \( u \) at time \( k \) when the system is in state \( i \). We assume that the terminal reward \( r(i, \cdot, N) \) is independent of the action chosen.
A policy is a sequence of functions $\pi = \{\mu_M, \ldots, \mu_{N-1}\}$, where each $\mu_k$ maps a state to an action in the action set $U$. The expected (total) reward, if the system starts in state $x$, over a finite time-horizon $N - M$ when applying the policy $\pi$ is

$$J_\pi(x) = \mathbb{E}\left[ r(x_N, \cdot, N) + \sum_{k=M}^{N-1} r(x_k, \mu_k(x_k), k) \middle| x_M = x \right].$$

The solution of an MDP is a policy $\pi^*$ such that

$$\pi^* = \arg\max_\pi J_\pi(x). \quad (1)$$

In words, the optimal policy $\pi^*$ tells us what action we should take at each time given the current state of the system, as to maximize the expected accumulated reward during the remainder of the time-horizon over which we are considering the problem. Note that any policy, in our setting, can be illustrated in a look-up table since the state-space and time-horizon are finite.

A complete treatment of MDPs, along with methods for solving problem (1), can be found in any of the standard textbooks; e.g., [3], [4].

III. MODEL

To formulate the AAA treatment problem in the above framework, we need to define the state-space, the reward function, the action set and the transition probabilities for an AAA. The objective is to determine an optimal policy $\pi^*$ that will maximize the expected number of QALYs to be accumulated over the patient’s remaining life. We make the assumption that there is a maximal age of $N = 120$ years and that the interesting interval for optimization is from an age of $M = 65$ years.

Due to available data, we let the time-step of our MDP be one year. The reward function $r(i, u, k)$ is defined to be the QALY equivalent of the age $k$ if the patient is alive, and zero otherwise. In other words, the reward gained in one year is one year compensated for the age of the patient. It should be noted that it is not at all obvious how this compensation should be calculated, however, that is the subject of other works, see, e.g., [11] and [14]. We let the quantized diameter of the AAA be the state of the system. The interval of quantization was chosen as 5 mm due to the available data (see the discussion on rupture and growth probabilities below). To make the MDP terminate in case of death by rupture, surgery or natural causes, we introduce an auxiliary terminal state (label: dead) and also a state for the system after successful surgery (label: no AAA). The state-space is therefore the set

$${\mathcal X} = \{\text{dead, no AAA, } 30 \text{ mm}, 30 - 35 \text{ mm}, \ldots, 70 - 75 \text{ mm}, 75 - 80 \text{ mm}, > 80 \text{ mm}\}. \quad (2)$$

We allow for two actions in our MDP model: $U = \{\text{continue surveillance, perform surgery}\}$. These two actions influence the transition probabilities of the system as can be seen in Figures 2a and 2b. Figure 2a illustrates the structure of the model if the choice of action is to perform surgery and Figure 2b shows the structure of the model if the choice of action is to not perform surgery (i.e., continue surveillance for one year).

To be able to compare our results to the current clinical policy, i.e., perform surgery if the diameter of the AAA is greater than 55 mm, it is illustrative to show how the current policy can expressed in the MDP framework. The policy $\pi_{55} = \{\mu_{55}^M, \ldots, \mu_{55}^{N-1}\}$ has $\mu_{55}^i = \mu_{55}^i$ for all $i = M, M + 1, \ldots, N - 1$ where

$$\mu_{55}^i(x) = \begin{cases} \text{continue surveillance} & \text{if } x \in \{\text{dead, no AAA}, \text{30 mm}, \ldots, 50-55\text{mm}\}, \\ \text{perform surgery} & \text{otherwise.} \end{cases}$$

The policy $\pi_{55}$ is graphically illustrated in Figure 3a where a black cell indicates that surgery should be performed and a white cell indicates that no intervention should be made.

Numerical values for the transition probabilities between different states and the reward function were obtained from the available literature on the topic, as discussed in the following. AAA is a disease that is most prevalent in males, and therefore most literature, and our scope, is limited to male patients. [14] synthesized evidence regarding aneurysm growth, rupture risk and age-dependent modeling of QALYs for a Markov chain model which evaluated the potential benefits from screening as compared to non-screening for AAA. The same parameters were used in our model. However, in [14], no rupture probabilities for AAAs that are smaller than 50 mm are reported. Hence, rupture probabilities for aneurysms with a diameter below 50 mm were retrieved from a systematic meta-analysis that complied rupture probabilities from 14 studies of small aneurysms [13].

Instead of the case of a ruptured AAA leading to certain death, we included in our modeling the chance of reaching a hospital and there undergoing successful emergency surgery. We considered only the surgical intervention called open surgical repair (OSR) of AAAs. Parameters, i.e., age-dependent surgical mortalities for both emergency and elective settings, as well as the probability of reaching a hospital, were retrieved from [15]. Data for age-dependent background mortality was collected from [16]. The above discussed parameters and their references are summarized in Table I.

IV. RESULTS

Table I: Summary of the parameters used in the model and the corresponding references.

| Parameter              | Reference | Parameter               | Reference |
|------------------------|-----------|-------------------------|-----------|
| Rupture probabilities  | [13]      | Growth probabilities    | [15]      |
| QALY, c                | [14]      | Surgical mortalities    | [15]      |
| Reaching hospital      | [14]      | Background mortalities  | [16]      |

Problem (1) was solved for the model outlined in the previous section using a Python implementation of dynamic programming. Data analysis and generation of plots were performed using the R programming language. Generating the
optimal policy takes approximately one second on a 3.2 GHz MacBook Pro.

The resulting optimal policy is illustrated in Figure 3b. It is clearly structurally different from the current policy which is illustrated in Figure 3a. In these figures, the horizontal axes show the size of the aneurysm, and the vertical axes show the age of the patient. A black cell indicates that surgery should be performed, and a white cell indicates that no action should be taken (i.e., continue surveillance for one year). The optimal policy shows that younger patients benefit from surgery at small diameters, and that the threshold diameter should be increased as the patient ages.

Figure 4a displays the total expected number of QALYs that are expected to be accumulated during the remainder of a patient’s life using the optimal policy. Figure 4b shows the improvement in terms of the difference in number of QALYs using the two policies in Figure 3.

As indicated by Figure 4b, an improvement of the number of QALYs can be expected. This improvement is most significant in patients aged 65 to 80 years with aneurysms sized 30 to 55 mm. There is also an improvement for older patients aged 105 to 120 with aneurysms sized 55 to 80 mm and above. The relevance for such old patients is, however, primarily hypothetical. These improvements are expected since the optimal policy differs from the current one for these patients. A small improvement in the number of QALYs can also be expected in the region that corresponds to patients aged 105-115 with aneurysms that are 50-55 mm in size. While the two policies here coincide, the optimal policy assumes optimal action in the future (when the AAA grows), that leads to an improvement.

There is a noticeable difference in the proposed policy with respect to at which age operation is the optimal treatment choice between aneurysms that are smaller and larger than 55 mm. This may be due to the fact that the only high

Fig. 2: Structure of the MDP illustrating the two Markov chains resulting from the two available actions; perform surgery and continue surveillance (for one year). The (age-dependent) probability of a transition is proportional to the thickness of the associated arrow.
quality evidence from controlled clinical trials for aneurysm growth and rupture rates relate to small aneurysms, whereas for large aneurysms only smaller case series with selected patient-cohorts are available. For an extended discussion, see Appendix A.

As always when using measured parameters in a model, it is of interest to evaluate how robust the results are with respect to the uncertainty in the parameters. To test the robustness of the calculated optimal policy, we generated random perturbations from the published data uncertainties on the rupture probabilities (from [14] and [13]). One thousand sets of parameters were generated and optimal policies were calculated for each set. The ratio of policies that indicated that a certain action should be taken at a certain age and aneurysm size is shown in Figure 5. It can be observed that the structural shape of the optimal policy is stable with respect to the perturbations of the parameters.

V. DISCUSSION

We have shown that a policy that optimally takes into account the expected remaining (quality adjusted) life-years of a patient and the age-related surgical mortality differs markedly from the policy which is currently used in clinical practice. The structure of the suggested policy is intuitively appealing: For a patient with less expected remaining life and a high operative risk, a higher AAA rupture probability (size) is demanded in order to take action.

The exact thresholds in the generated policy may not be clinically applicable yet. They are subject to change as better estimates of the model parameters become available from clinical studies. However, as shown, the structure of the policy is robust to perturbations in the current model parameters which indicates that even if the exact threshold values are not determined yet, the structure of the currently used clinical policy is sub-optimal and demands further investigation.

As previously mentioned in Section II the current policy has been studied in randomized controlled trials and has been shown to be associated with a lower mortality than a policy where small (40-55 mm) aneurysms are also operated [2]. These trials, however, did not have sufficient power to perform sub-group analyses with regard to age or gender [2], and could thus not demonstrate the results suggested here, i.e., that smaller aneurysms should be operated in young patients.

There are many extensions that could be made to the work presented in this paper. We considered only age-dependent surgical mortality that is related to open surgical repair. It would be interesting to include, by extending the action set $U$, other types of surgical interventions. A time or state dependent $U$ could limit some of these surgical methods to certain ages or certain AAA diameters. Post-operative complications can also be introduced in the model by the addition of new states.

It should be noted that, in this paper, age can partially be viewed as a surrogate marker for co-morbidity. It is possible to identify patients with increased operative risk (due to co-morbidities) using, for example, the score proposed in [17], or patients with an increased rupture risk (e.g., women or patients with a family history of ruptured AAAs), for whom individual risk parameters can be used to generate patient-specific policies. It may also be relevant to improve patient-centered decision making by allowing patients themselves to estimate QALYs.

Also, as more specific markers for AAA rupture and growth (e.g., biomechanical rupture risk markers from finite element analysis [18]) become clinically available, policies will have to
be re-established to include such data as basis for the decision. Such new policies, we believe, should be synthesized with the help of mathematical methods for decision-making. The MDP framework admits new markers to be incorporated by either an extension of the state-space or by extending the framework to partially observed MDPs (POMDPs) [19].

A. Related work

In the context of healthcare, the MDP framework has been used to provide guidelines for decisions in such disperse settings as ambulance scheduling [20], planning the treatment of ischemic heart disease [21] and kidney transplantations [22]. For a more extensive overview of healthcare related applications of MDPs, see for example [23] and references therein.

The question of improving the treatment policy for AAAs using mathematical modeling has been considered before. However, the MDP framework has, to the knowledge of the authors, not been used before. The structure of our policy is similar to the one recently obtained in [24] using a Markov model where different treatment options were evaluated against each other by simulating their outcome over a large cohort of (virtual) patients. However, in contrast to enforcing a surgical intervention at different AAA diameters and comparing the simulation outcomes, the MDP framework a) uses analytical expression for expectations, which bypasses the need for approximations using simulations and makes the computation of the solution more efficient. It also b) generates a policy that takes into account that the surgeon will act optimally in the future due to the principle of optimality [25]. This means that we include the possibility of not performing surgery now, since we know that it will be performed at a later stage, when generating the policy. A more elaborate discussion regarding this is available in [26]. Moreover, we believe our framework allows the extensions discussed in the previous section to be made more easily.

VI. Conclusions

In this paper we have demonstrated how methods from operations research on sequential decision making can be employed for weighing risk against potential benefit in the case of AAA treatment. We have demonstrated that a patient-specific policy outperforms the currently used policy. Our results indicate that the optimal treatment policy might be of a more complex form - age and size dependent - than the one that is employed today. In particular, smaller aneurysms should be operated in younger patients. These results warrant further investigations into a policy that is age dependent.

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APPENDIX A

REGARDING THE RUPTURE RISK FOR LARGE (> 55 MM) ABDOMINAL AORTIC ANEURYSMS

As mentioned in the results section of this paper (i.e., Section IV), the abrupt change in the policy at 55 mm is somewhat unexpected. We mentioned that such a discontinuity likely corresponds to a bias in the data. In particular, that either the rupture risk for large aneurysms is estimated as disproportionally high, or that the rupture risk for small aneurysms is estimated as disproportionally low.

After publication of this manuscript, it has been proposed in [27], that the rupture risks presented in the literature for large aneurysms are overestimates. In particular, [27] indicates that rupture risks for aneurysms between 55 and 69 mm are overestimated. With respect to our results, this would lead to a bias in the policy, such that larger aneurysms are disproportionally avoided (i.e., operated). This would manifest itself as an abrupt change in the policy for aneurysms of size 55 mm and larger – exactly as is apparent in Figure 3. Thus, we believe that our results also point to possible previous overestimation of rupture risks for large aneurysms.

Additionally, we note that the sensitivity analysis presented in this paper only demonstrates the stability of the policy with respect to variance in the parameters and would therefore not be able to detect the systematic bias proposed in [27].