

Implications in the treatment of peripheral arterial disease

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1. (Research) What is the main objective of the research described in the thesis and what are the most important results and conclusions?

The main objective of the research in this thesis is to get an insight and quantify side effects of several treatment strategies regarding peripheral arterial disease (PAD). Moreover, how can we anticipate or abolish these side effects. For instance; endovascular treatment of PAD requires the use of iodine contrast and radiation to image arteries, which are damaging to several organs, such as skin and kidneys. Therefore, first line treatment of PAD on initial presentation is supervised exercise therapy (SET), whereas this is a non-invasive strategy. We demonstrated that renal function after one year declined significantly more in patients treated with an endovascular procedure, when compared with SET. Also, long-term renal function is significantly worse in patients treated with an endovascular intervention when compared to open surgery. The worsening renal function is a supposed consequence of iodine contrast. Moreover, radiation exposure is known to cause potential acute and/or long-term effects on penetrating tissue (skin, muscle). To get a better understanding of which anatomical region is most at risk we quantified the used radiation doses and cumulative time of radiation in several procedures. This thesis showed that the radiation exposure is highest in arterial treatment of arteries in the pelvic area and the thigh, when compared to the more distal regions. The more tissue to penetrate imaging the arteries, the higher the radiation dose.

To address these issues, we investigated ways to decrease the detrimental effects and studied novel approaches to completely eliminate these effects, without compromising in outcome. We studied the possibility of treating a clothed artery in de legs with balloon dilatation using ultrasound as an imaging technique. The results showed no difference in success compared to the conventional imaging technique using contrast and radiation. Furthermore, this thesis quantified renal function before and after an intervention. No significant decrease in renal function was observed in either treatment group. This is possibly explained by adequate fluid therapy, improvement in imaging techniques and iodine contrast. However, patients with poor renal function before an intervention are at increased risk of renal decline after the use of iodine contrast. Using fluid therapy, concentration of iodine contrast in the kidneys is diluted. Preferably a high and steady urine production is achieved, without risking excess fluid administration. To achieve high urine output, diuretics can be administered. However, there is an increased risk of

fluid depletion and thus increasing iodine contrast concentration and possible damage to the kidneys. To achieve the right balance of administered fluids and diuretics is difficult. Therefore, we designed a study protocol using the Renalguard. This is a little device which weights the urine produced and administers fluids accordingly to achieve an increased and steady flow over the kidneys. This study will examine the benefit of the Renalguard compared to conventional fluid therapy in patients treated endovascularly for PAD.

Finally, as mentioned earlier SET is the initial treatment regarding intermittent claudication. However, even though great improvement of walking distance can be achieved when dedicated to the therapy, adherence to SET is low. We tried to identify reasons for low adherence and identified several relevant behavioral determinants. It appeared knowledge, attitude and self-efficacy are of great importance and need to be addressed to improve adherence to SET.

2. (Relevance) What is the (potential) contribution of the results from this research to science, and, if applicable, to social sectors and social challenges?

The contribution of the results from this science is plural. It gives an insight in the long-term effects of endovascular procedures for intermittent claudication and critical limb ischemia on renal function. Furthermore, we determined radiation exposure in different anatomical locations of patients treated with endovascular interventions of the lower extremities. We provided a good alternative for endovascular treatment of the groin area in patients with diminished renal function without having to rely on contrast agent. The results disputed the arguments of any hindrance of duplex visualization due to bowel gas or obesity. The research also suggests a possible solution in furosemide forced diuresis, which also limits the harmful effects of iodine contrast on kidneys. To prevent an invasive intervention altogether, physicians need to increase a patient's knowledge and attitude toward PAD and SET. This might aid physicians and patients to improve adherence to SET and avert an invasive procedure.

3. (Target group) To whom are the research results interesting and/or relevant? And why?

The research results are mainly interesting and relevant for vascular surgeons and interventional radiologists treating patients with PAD in the lower extremities. Results might also be relevant for general practitioners, in particular how to approach a patient on initial presentation with intermittent claudication. The general practitioner often has a closer and more frequent contact with a patient. This might result in a greater influence on a patient's behavior and thus be more inclined to take the general physicians advise.

4. (Activity) In what way can these target groups be involved in and informed about the research results, so that the knowledge gained can be used in the future?

These target groups are and can be informed by presenting these study results on national and international conferences. Furthermore, the studies in this research are published in international journals.