Utilization of MR-venography in deep vein obstruction

Chapter 10: Impact paragraph

In this chapter, the relevance and the socio-economic, clinical and scientific impact of the research described in this thesis is discussed. The research in this thesis was performed over the course of the past decade. Our knowledge and understanding of deep venous system imaging interpretation have expanded with each year and each chapter of this thesis. After completion of the CAVA trial the full scope of our magnetic resonance venography (MRV) approach became clear, in particular how it could affect clinical management of (acute) deep vein thrombosis. At the same time it may be that, even after a decade of evolution in our views and interpretations, we have only 'scratched the surface' of imaging deep venous disease.

Socio-Economic impact

As it stands, evaluation of lower extremity deep vein thrombosis with duplex ultrasound (DUS) provides a good medical imaging tool to support an optimized referral pathway. Based on current criteria and guidelines the outcome of a diagnostic DUS generally leads to correct referral for patients. We should however not underestimate the current socio-economic impact of deep vein thrombosis with its associated high morbidity and long-term complications, which not only affect patient QoL but also impose a financial burden on society. This holds true in particular for the development of post-thrombotic syndrome (PTS) after acute deep vein thrombosis. PTS is a complication that occurs in 40% to 60% of deep vein thrombosis patients when treated according to the current guidelines.[1,2] It has serious negative implications for the quality of life and contributes to rising healthcare costs.[3,4] In view of these facts, developing and implementing more advanced (non-invasive) imaging tools like MRV provides an opportunity to ensure an early and more precise diagnosis, essential for treatment success and prevention of (long-term) complications. In this thesis we have shown that, for patients with extensive iliofemoral deep vein thrombosis, MRV can provide additional imaging information to help guide an optimized treatment plan, which potentially reduces therapy associated risks and costs since invasive treatment can be applied in those with potential high yield and avoided in those with expected low yield.

Clinical impact

Deep venous thrombosis is a complex disease in which the main contribution of imaging is and has been the evaluation of the presence or absence of a deep vein thrombosis. Most efforts have been invested in supporting the treatment of deep vein thrombosis with anticoagulant therapies.[5,6]

With the publication of the first successful studies on minimally invasive, catheter-directed thrombolysis (CDT) for deep vein thrombosis between 1995 and 2000 a renewed interest in thrombolysis as treatment option for deep vein thrombosis was created.[7,8] The first randomized

controlled trial, the CaVent study, underlined the potential of catheter directed thrombolysis for the prevention of the post-thrombotic syndrome.[9] However, this trial and consequent trials did not deliver on this promise.[10,11] It was argued that adequate patient selection could be an important contributor to success of the intervention. Furthermore, it was argued that CDT in addition to anticoagulation was only the starting point of the treatment. Without treating any underlying obstruction, the potential benefits regarding outcome will be suboptimal. The aim of the CAVA-trial was to focus on evaluating and treating iliofemoral deep vein thrombosis. At that time, experts considered duplex ultrasound and venography the only established imaging modalities for deep vein thrombosis. We included MRV in our evaluation of patients suspected of iliofemoral deep vein thrombosis which contributed to the awareness of underlying deep venous disease (deep vein stenosis and / or chronic obstruction) as an important factor for (long-term) clinical success. More importantly we developed an imaging assessment technique that allows for virtual thrombus aging based on imaging alone, providing a prognostic tool for CDT success or failure. This technique proved to yield a clinically relevant parameter which can be used by clinicians to decide when (not) to opt for CDT, minimizing unnecessary patient exposure to the risks of CDT. Additionally virtual thrombus aging reinforced the concept of treating (iliofemoral) deep vein thrombosis as soon as possible since this ensures the shortest required thrombolysis time.

Current medical practice shows that patient selection and treatment is relying more and more on medical imaging information. Our MRV protocol will enable radiologists to better consult their clinicians in selecting patients eligible for venous interventions. Our MRV protocol can thus help the selection process and treatment of deep vein thrombosis patients and benefits patients directly.

Scientific impact

Deep vein thrombosis is a relatively common disease, both spontaneous and after surgery.[12] Identifying deep vein thrombosis early is of great importance in improving outcomes for patients by preventing pulmonary emboli, extension of deep vein thrombosis and reduce long-term risks such as PTS.[13-15] In this thesis we have shown that we could improve outcomes by adding MRV to the diagnostic algorithm for patients with iliofemoral deep vein thrombosis, and that MRV can help guide therapy choices by interpreting imaging characteristics of thrombus. This information is useful for both clinicians and researchers as it represents 'a piece of the puzzle' for the explanation of the (lack of) long term success in treating deep vein thrombosis with CDT. Completely unraveling the pathophysiology of DVT might be out of reach, but medical imaging can contribute to the evaluation of treatment strategies for deep vein thrombosis patients. Introducing MRV as part of the routine assessment of (extensive) iliofemoral deep vein thrombosis currently has limited clinical applications. We managed to present an MRV image interpretation technique useful as a non-invasive diagnostic tool to assess virtual thrombus morphology, thereby creating the possibility of future MR imaging

research on imaging-based deep vein thrombosis assessment and treatment. As outlined in the discussion, a potential research application would be detailed analysis of MR imaging features in the acute phase coupled with histological clot analysis.

MRV has long been considered inaccessible or highly complex and reserved for academic specialty centers only. In this thesis we demonstrated the potential of performing MRV on a mainstream 1.5T MRI machine, with an acceptable exam duration, utilizing a regular gadolinium-based contrast agent. Both the reduction in acquisition time and the alternative for more complex contrast agents deemed mandatory in the past (and now virtually unobtainable) improved accessibility and utilization of MRV for deep vein thrombosis. With less requirements, more sites can participate in both research and clinical utilization of MRV.
There is a rapid expansion of new minimally invasive treatment options for thrombus removal. When to use these techniques or how pre-interventional imaging can guide (technical) treatment choices has yet to be established. The virtual thrombus aging imaging technique described in this thesis could already be used to evaluate the use of pharmaco-mechanical and strictly mechanical thrombectomy devices which have been introduced in recent years.

This thesis shows that there is potential to improve on the imaging work up in deep vein thrombosis patients by performing MRV, when considering treating these patients with minimally invasive techniques, such as catheter-directed thrombolysis and/or stent placement. Current data do not support routine implementation of catheter directed thrombolysis in clinical care. However, the expectation is that there is room for improvement and better results might be achieved by better patient selection, better device selection and more supportive treatment after initial care, so that long-term risks of minimally invasive thrombolysis and/or thrombectomy will ultimately outweigh the gains.

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