The diagnostic potential of 18F-Fluoride PET/CT in lumbar spinal fusion patients

Valorization

Low back pain is a major global health and economic problem [1,2], with a one-year prevalence ranging from 22 to 65% and life-time prevalence of up to 84% [3]. It is the leading cause of activity limitation and work absence [4, 5], as well as a huge economic burden. Costs associated with low back pain include direct costs for health-care and indirect costs because of work absenteeism [6]. The total societal cost of low back pain in the Netherlands is 4.88 billion USD of which 12% accounts for direct medical costs and 88% for indirect societal costs [7]. Total cost per person in the Netherlands is 300 USD of which 36 USD is direct cost and 264 USD is indirect cost [7]. The total societal cost in the USA is 81.24 billion USD of which 47% accounts for direct medical costs and 53% accounts for indirect societal costs [8, 9]. Total cost per person in the USA is 308 USD direct costs and 145 USD indirect costs [8, 9]. The problem of low back pain is expected to continue to grow as a result of the aging and increasing population worldwide [5]. When conservative measures to treat low back pain, such as intensive exercise therapy, pain medication or brace immobilization fail, operative intervention can be considered. Spinal fusion is a surgical procedure in which fixation of vertebral segments is achieved by means of instrumentation and bone grafting to treat patients suffering from back pain. Pain relief is achieved by restoration of the height of the segments, decompression of the nerve roots and definite bony fusion of the vertebrae involved. Unfortunately, 5 to 50% of patients will suffer from persistent or recurrent back and/or leg pain after spinal surgery [10]. Pseudarthrosis or non-union is thought to be the cause of pain in a significant number of spinal fusion patients with persisting or recurrent symptoms [11, 12]. However, pseudarthrosis can also be asymptomatic [12-14]. In that sense, the value of imaging modalities that allow for detection of pseudarthrosis such as CT and radiography, can be limited in spinal fusion patients with complicated pain symptoms.

In this thesis, the use of ^{18}F-fluoride PET/CT scanning in patients early after spinal fusion as well as in patients with persistent or recurrent symptoms several years after fusion surgery, was evaluated. The most important findings were that static ^{18}F-fluoride PET/CT findings in patients with persistent or recurrent pain after spinal fusion, correlated better with symptoms than CT findings do, and that as early as six weeks after surgery, differences in bone metabolism can be detected between patients developing pseudarthrosis and fusion at one year after spinal fusion surgery by means of dynamic ^{18}F-fluoride PET/CT scanning.

Application of ^{18}F-fluoride PET/CT in clinical practice

In the studies in this thesis, ^{18}F-fluoride PET/CT was not used for clinical decision making yet. In follow-up studies, we would like to base treatment after spinal fusion on PET/CT findings. For example, hotspots at facet joints could indicate a facet joint block and severe hotspots at the endplates could be an indication for revision surgery. When subsequently improved clinical follow-up results or even confirmation of PET/CT findings by observation of abnormalities during revision surgery can be shown, ^{18}F-fluoride PET/CT could be advocated to be incorporated in clinical practice of patients with persistent or recurrent pain after spinal fusion. This would potentially lead to more efficient treatment plans at an earlier time point, resulting in less uncertainty and shorter periods of limitation in daily life activities for the patient. At present, ^{18}F-fluoride PET/CT is not yet available in all hospitals. Less advanced nuclear techniques such as a technetium bone scan including SPECT/CT, are widely available and may be used as surrogate parameters [15]. Given the closer correlation with symptomatology, a SPECT/CT or PET/CT scan may be advocated as a routine procedure in patients with persisting symptoms after spinal fusion.
Economically, better diagnoses of patients with pain after spinal fusion amounting to more efficient treatment plans would decrease the direct costs for health-care as well as the indirect costs as a result of work absenteeism.

^{18}F-fluoride PET/CT as a diagnostic research tool

By means of dynamic ^{18}F-fluoride PET/CT, parameters related to bone blood flow and bone incorporation can be calculated which can give prognostic information in an early phase after spinal fusion. The direct clinical value of this information is limited as of yet, but the technique can be used in a (pre)clinical research setting. By means of dynamic ^{18}F-fluoride PET/CT scanning, equality or superiority of alternative graft materials to autologous bone grafts in the early postoperative phase can be demonstrated in clinical research studies. Besides alternative bone grafts, new cage designs or screws can also be evaluated. The PET/CT imaging technique can also be used as a diagnostic tool in preclinical studies. Preclinical models give the liberty to make more standardized comparisons and allow for confirmation of findings by means of histological analysis.

Besides multiple research designs that can be thought of regarding spinal fusion, the ^{18}F-fluoride PET/CT technique can also be applied to other areas where changes in bone metabolism are of value. For example, different types of fracture healing or osteotomy can be evaluated. Furthermore, several metabolic diseases such as rheumatoid arthritis, Paget's disease, osteoporosis and osteoarthritis could be studied. ^{18}F-fluoride PET/CT could also be used to distinguish between septic and aseptic loosening of different types of prostheses, for example hip prostheses [16] or knee prostheses [17]. Prostheses designs

nowadays are focusing more and more on early ingrowth, which is a challenge to demonstrate with common imaging modalities. Research with ^{18}F-fluoride PET/CT and its clinical application for multiple conditions can go hand in hand and consolidate each other.

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