Sequence of segmental contributions in the lower cervical spine and their application to cervical arthroplasty

Valorisation

The mean annual incidence of cervical radiculopathy is reported to be about 83 per 100,000 people, with a peak incidence of 202 per 100,000 for people aged 50 to 54 years. The prevalence is about 3.5 per 1,000 people, also with a peak in the sixth decade [1, 2].

The natural course of a cervical radiculopathy is benign, with a spontaneous resolution of complaints in 60% of the patients after 6 weeks of conservative treatment, and in 83% of the patients after 2 years of conservative treatment [3]. A recurrence of a cervical radiculopathy has been described in 31.9% of the conservatively treated patients. Many of these were isolated recurrences [1]. The reported proportion of patients who are eventually treated surgically ranges from 8% to 35% [1, 4, 5]. In the Netherlands, around 2,000 patients with cervical radiculopathy are operated upon each year. Based on these numbers, the cost of surgical treatment of cervical radiculopathy was estimated to lie around 30 million euros [6]. Of the surgically treated patients, around 90% was satisfied with the result at 6 to 8 weeks after surgery [7-9].

Although many of the patients recover from the complaints with conservative therapy alone or with surgical treatment, the burden of disease is high in these patients whilst the complaints are still present. The actual burden of cervical degenerative disc disease for society is not known. The costs-of-illness for neck pain in the Netherlands have been reported to be 1% of the total health care expenditures in 1996 [10], the largest part of these costs were related to disability and absenteeism (35% and 65%, respectively). The percentage of these patients with neck pain that had a cervical radiculopathy is not reported. The largest company in the Netherlands that supports employers and employees in illness-related absenteeism, ArboNed, reported a total of 1079 people absent from work due to a cervical radiculopathy in the period 2015 to October 2018. This was about 1.2% of the total amount of people that were reported to be absent from work in that period. On average, they were absent from work for 246 days (personal communication with ArboNed). One day of absence from work is usually calculated to cost around 250 euros, which leads to average costs of absenteeism of 61.500,- euros per patient. Given that the market share of ArboNed lies around 23%, the actual number of patients that were absent from work during that period due to a cervical radiculopathy can be extrapolated to be four times higher, with annual costs solely due to absenteeism of 66 million euros.

An RCT investigating cost-effectiveness in ACDF and dorsal foraminotomy in cervical radiculopathy is currently including patients, and could shed more light on the actual societal cost of cervical radiculopathy [11]. This will of course only be applicable to a subset of patients, the ones who end up being surgically treated. Another RCT investigating cost-effectiveness of three types of surgery for cervical radiculopathy, 1) ACD with interbody fusion, 2) ACD without interbody fusion and 3) arthroplasty has finished including patients, but results have not been reported yet [12].

Secondary surgery

The incidence ASDis in patients who have undergone fusion surgery is reported to be 2.9% per year, and 25% in ten years [13]. Prevention of new radicular complaints in surgically treated patients could prevent new episodes of discomfort, disability, absenteeism, as well as the accompanying costs. If there are differences in cost-effectiveness between the different surgical treatments of cervical radiculopathy the studies mentioned in the previous paragraph can hopefully shed more light on it [11, 12]. Given the fact that the intended goal of cervical arthroplasty is preventing secondary complaints due to adjacent segment disease (ASDis) the societal burden in the long term could be lower in the arthroplasty group.
The idea behind cervical arthroplasty is to reduce adjacent level surgery by preserving motion in the operated segment. This thesis, however showed that the imaging technique is very good, but interpretation of normal motion remains difficult. An actual reduction in ASDis can only be proven with long-term randomized studies of good quality. Long-term data are slowly becoming available and several of them report lower rates of secondary surgery in the arthroplasty group, when compared to the fusion group [14]. We are currently performing a systematic review on the long term results of RCT's comparing arthroplasty to fusion [15]. This will hopefully shed more light on this subject. However, irrespective of a difference in secondary surgery that might be present, it is yet unknown whether this can be linked to the postulated preservation of motion.

Timing of evaluation

A reduction of secondary surgery is based on the assumption that arthroplasty preserves physiological motion, and that fusion plays a causal role in the development of ASDis. A definition of a physiological motion pattern was reported in this thesis. This motion pattern was present in most asymptomatic individuals, while absent in the majority of CDDD patients. It was present in the majority of these patients after surgical decompression with placement of a cervical disc prosthesis.
Although this is only one parameter of physiological motion there currently is no alternative that can differentiate more reliably between CDDD patients and asymptomatic individuals. It could therefore be used as a tool to evaluate patients after surgery. While clinical results take 5 to 10 years of follow-up (and even then a systematic review appears to be necessary to be able to reach statistical significance), the motion pattern of a patient can be determined one year after surgery. However, to be able to draw conclusions based on the sequence of segmental contributions data from one year after surgery, a good correlation would have to be shown between the motion pattern and long term outcome.

To determine whether this method is useful as an early parameter to determine if a type of prosthesis (or other variables such a location of the disc prosthesis within the disc

space, or concomitant degenerative changes) facilitates a physiological motion pattern, a much larger sample size would be necessary given the low annual incidence of ASDis and the large amount of variables that might influence results. Ideally this method of analysis would be used more widely, in future (or ongoing) RCT's.

It has already been shown that cervical arthroplasty preserves motion in the majority of patients, primarily by use of segmental range of motions (sROMs). Given the known high variability of sROMs the data are not useful to determine if *physiological* motion is present or absent. Without information whether the motion is physiological or not, it cannot be concluded that motion preservation on itself might be enough to prevent secondary surgery. It is possible that patients with a physiological motion pattern have a lower risk of secondary surgery then patient with preserved motion but without a physiological motion pattern.

Expertise in analysis of sequence of segmental contributions

There are several companies (e.g. Medical Metrics Inc., ICON) that offer analysis of various types of imaging such as digital subtraction angiography (DSA), X-ray CT, single photon emission computed tomography (SPECT), positron emission tomography (PET), optical techniques and magnetic resonance imaging (MRI). These Imaging Core Labs (ICLs) support trials by collecting, analysing (blinded) and archiving the imaging data for a complete trial. Some of these ICLs are commercial, others are academic / not-for-profit. In the fusion and arthroplasty studies these companies primarily analyse flexion- and extension radiographs (to determine sROMs and translations in the sagittal plane). As was stated above, these outcomes are less than optimal for use in individual patients. None of these ICLs currently offer analysis of sequence of segmental contributions.

A similar type of Imaging Lab could be set up to offer analysis of sequence of segmental contributions. Facilitating use of this method of analysis in other studies could help to make it more widely used.

Impact for future health care if a relation between preservation of physiological motion and secondary surgery would be proven

If a physiological motion pattern would be proven to correlate with a decrease in the risk of secondary surgery there could be a role for analysis of sequence of segmental contributions in earlier stages of clinical trials of new types of cervical disc prostheses. Because the sequence of segmental contributions can be determined one year after surgery, while results on secondary surgery take several years (and large groups) to become known, valuable time and resources could be saved. If a new type of prosthesis preserves motion, but without a physiological motion pattern, design changes could be implemented.

Ideally, one would want to be able to do this even before clinical trials, in the design phase. It would then be necessary to find out which parameters determine the physiological motion pattern (e.g. the location of the centre of rotation of a prosthesis, whether or not it needs to be able to accommodate translation in the coronal/sagittal/transverse plane, but also patient specific variables such as the size and shape of the intervertebral space, orientation and shape of the facet joints, and alignment of the spine). A very large amount of source data would be necessary to determine this, which is not realistic at this time. A second option would be a combination with Finite Element Analysis to create a model of the cervical spine in which the influence of the parameters that were mentioned in the previous paragraph on the sequence of segmental contributions can be determined, and to validate this model using already available data. However, a highly complex model would be required to be able to do this.

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