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Intervertebral (lumbar) disc replacement: the current state and future perspectives

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Abstract

PURPOSE: Low back pain is a significant socio-economic problem which is expected to deepen. Degenerative disc disease is considered to be one of its main causes. Unsuccessful conservative treatments usually lead to surgical treatments, including methods providing pain relief by vertebral fusion in the affected segment. However, this leads to changes in biomechanics, which is why approximately 30 years ago total disc replacements appeared. This work aims at determining the current state of treatments with this kind of replacement, comparing the results with those of fusion methods and assessing why fusion continues to dominate. Current treatments of degenerative disc disease by advanced procedures (regenerative and gene therapy, 3D printing) is also examined and evaluated, and future developments are considered.
METHODS: A critical review based on available scientific articles from online databases. The main keywords used were „lumbar", „total", „disc" and „replacement", supplemented according to the individual, monitored areas ("follow-up", "fusion", "future" etc.). For the articles found through database search (n = 895), narrower selection was made and the result was 33 articles included in review.
REVIEW: Total disc replacements have not yet satisfactorily demonstrated that they are superior to fusion methods in long term follow-up. Advanced methods are in their infancy.
CONCLUSIONS: Additional research and development of total disc replacements is still necessary. For implants, the 3D scan – 3D model – 3D printing chain and its related technologies are increasingly important. The development of regenerative procedures using induced pluripotent stem cells and gene therapies is important, but conservative treatments and primary prevention should also be developed because regenerative procedures and gene therapies apparently will not be used routinely until the future.

Abbreviations:

%	- percentage
3D	- three dimensional
4D	- four dimensional
AI	- Artificial Intelligence
ASD	- Adjacent segment degeneration
CE	- Conformité Européene
CRISPR	- Clustered Regularly Interspaced Short Palindromic Repeats
CT	- Computed Tomography
DDD	- Degenerative disc disease
e.g.	- exempli gratia (for example)
etc.	- et cetera (and so on)
iPSCs	- Induced pluripotent stem cells
LBP	- Low back pain
LDDD	- Lumbar degenerative disc disease
LTDR	- Lumbar total disc replacement
MRI	- Magnetic Resonance Imaging
MSCs	- Mesenchymal stem cells
ODI	- Oswestry Disability Index
R&D	- Research and development
RCT	- Randomized controlled trial
TDR	- Total disc replacement
VAS	- Visual Analog Scale

INTRODUCTION

Degenerative disc disease (DDD) is considered as one of the leading causes of frequently occurring low back pain (LBP) (Beatty 2018, Cui *et al.* 2018, Zigler *et al.* 2018, Bai *et al.* 2019). LBP impairs the ability of an individual to function normally in society and, therefore, represents a significant socio-economic issue (Büttner-Janz *et al.* 2014, Mattei *et al.* 2017, Salzmann *et al.* 2017, Gadia *et al.* 2018, Pimenta *et al.* 2018). Although the causes of LBP/DDD are considered to be multiple e.g. excess weight, smoking, heavy-duty job and sedentary job (Karaarslan *et al.* 2017), a lack of physical activity or, conversely, overloading, an unhealthy lifestyle and other factors, including genetic ones (Panska *et al.* 2016) and sometimes difficult to determine, a link to older age is considered to exist (Beatty 2018, Pimenta *et al.* 2018, Othman *et al.* 2019). Therefore, this problem is expected to deepen in aging populations (Salzmann *et al.* 2017).

In clinical practice, there are many procedures of treatment for LBP/DDD, including efforts to standardize them into guidelines. However, there is still no general consensus among physicians, and practices often differ significantly from existing guidelines (Foster *et al.* 2018, Zigler *et al.* 2018). Treatments may be divided into the surgical solutions and conservative approaches. Conservative approaches mainly include changes to activity, rehabilitation, muscle strengthening and the use of various drugs. In patients, who are not satisfied with regular medical care, alternative methods such as acupuncture are also used (Ondrejkovicova *et al.* 2017). If DDD does not cause acute neurological problems, conservative treatments are used as the first option. The duration of this treatment is individual and is reported to range from 3 months to 2 years (Mattei *et al.* 2017, Zigler *et al.* 2018). If LBP persists (20 % to 30 % of cases according to Othman *et al.* 2019), surgical treatments are usually turned to. One of the most common methods using implants is so-called "fusion" and aims to induce a firm bone tissue connection between vertebral bodies in the affected segment through the space of a partially extracted disc. In addition to the risks of the operation itself, this treatment brings with it changes to the biomechanics in the given segment, which may be a source of complications later. Among these complications, Adjacent Segment Degeneration – ASD is often mentioned (Salzmann *et al.* 2017, Cui *et al.* 2018, Pimenta *et al.* 2018). For this reason, implants for total disc replacement (TDR) appeared in the 1980s, which aim to maintain the movement in the operated segment. Even nowadays, more than 30 years later, however, the fusion method remains the so-called "gold standard" of surgical treatments using implants (Park 2015, Mattei *et al.* 2017, Wuertinger *et al.* 2018).

The aim of this critical review is to study the available scientific journal articles in order to determine the current state of TDR treatments focusing on the long-term results and their comparison with the results of fusion methods, to evaluate this state and consider appropriate future developments. Part of the work is therefore a basic overview of the current state of treatment using advanced methods and technologies. However, because it is clear even without a more detailed study of the literature that the best replacement for the patient is one that is not actually needed, prevention is also a topic.

MATERIALS AND METHODS

As the purpose of this article is to collect the current available information on the chosen topic, it is designed as a review based on scientific articles. The search was performed primarily in the PubMed (MEDLINE) database and secondarily in the Web of Science, Science Direct and BioMed Central. Additional Google searches of articles were also made. The main keywords used were „lumbar", „total", „disc" and „replacement", supplemented according to the individual, monitored areas. These were the present – in particular: „follow-up", „outcomes", „adverse", „spine", „fusion", „comparison", „low back pain", „prevention" and the future – in particular: „future" and advanced methods in the medical engineering: „three-dimensional", „printing", „tissue-engineered", "regeneration", „gene", „therapy", „editing" and „artificial". The reference period was from 2012 until the creation of this text. The rough selection of articles, found using the above-mentioned keywords and their combinations, was based primarily on the full title and then the abstract. An important criterion for the inclusion of the article in the basic selection was also the full text being in English as well as its direct accessibility in the database. For the available articles from the basic selection (n = 895), another, narrower selection was made on the basis of a more detailed examination

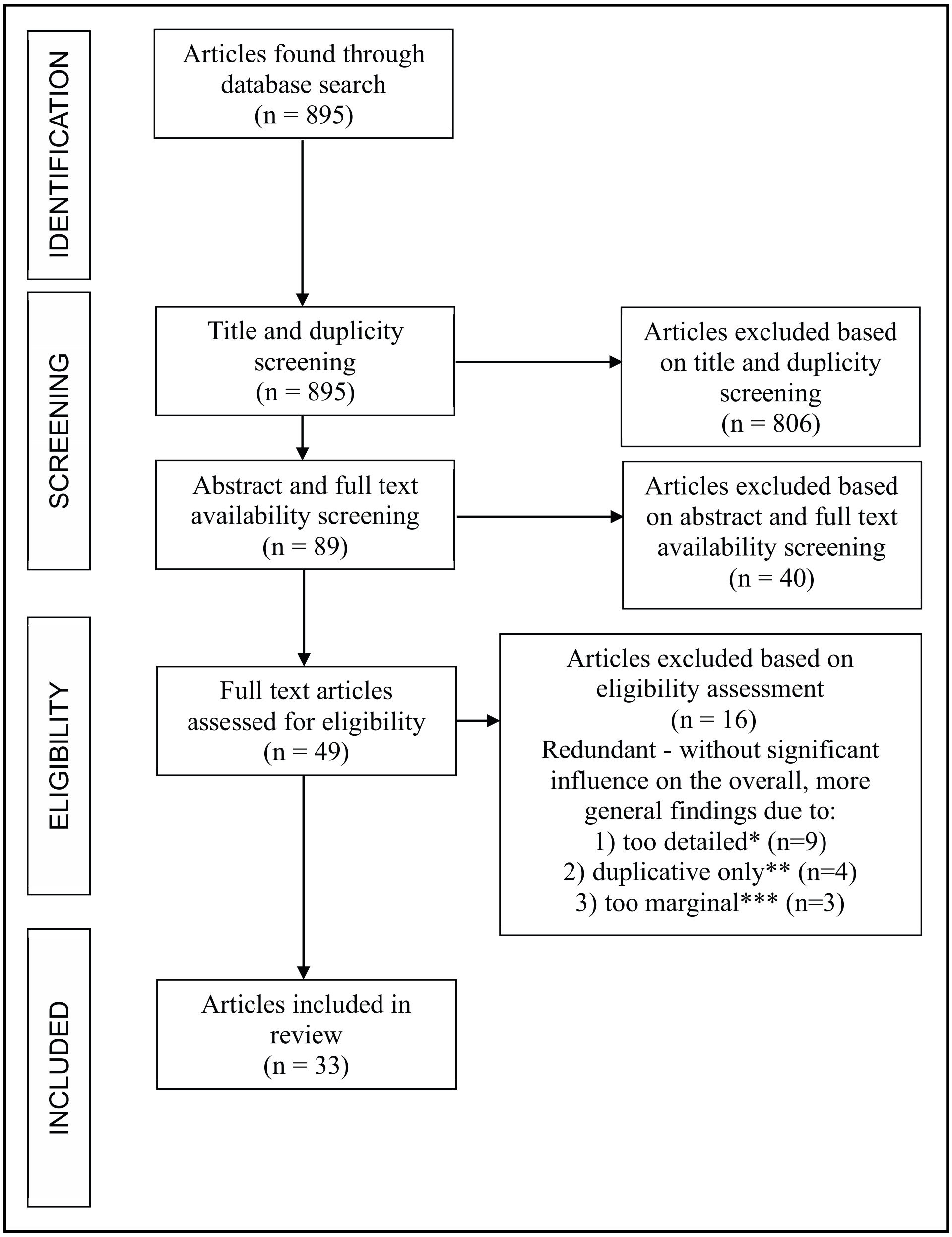

Fig. 1. The flowchart describing the articles' evaluation process

*The article only focuses in detail on the already known subtopic;
**The article merely duplicates information already found;
***The article touches on the subject too peripherally

of the full text. The resulting 33 articles (see Fig. 1 for the flowchart of the evaluation process) are hereinafter referred to as the "selected" articles and citations are used from them, which refer to the References section.

REVIEW

Brief overview of current state and future perspectives, described in subchapters in more details, is summarised in Table 1.

Disc replacements and their current results

The first generation of commercially-used lumbar TDRs appeared in the 1980s. The longest average follow-up of implantation results in the selected articles was about 17 years for the Charité implant (Cui *et al.* 2018, Carlson & Giblin 2022), but the usual periods are generally much shorter – e.g. Balboni *et al.* (2022) stated that two-year follow-ups are widely considered to be the gold standard when evaluating surgical success. Several authors aimed to include in their evaluation of the medium and long-term results the follow-ups which lasted at least 3 to 5 years (Park 2017, Salzmann *et al.* 2017, Cui *et al.* 2018, Wuertinger *et al.* 2018). The age of patients who underwent TDR surgery in the selected articles varied widely with the average age being for example 45 years (range from 29 to 66 years in Wuertinger *et al.* 2018). The results and therefore the success of treatments were measured mainly using questionnaires VAS (Visual Analog Scale) for pain and ODI (Oswestry Disability Index) for the limitation of patient mobility (Salzmann *et al.* 2017, Cui *et al.* 2018, Pimenta *et al.* 2018).

Tab. 1. Brief overview summarising main points of the current state and future perspectives – Intervertebral (lumbar) disc replacement

CURRENT STATE AND FUTURE PERSPECTIVES	It is understandable that fusion remains the gold standard for the surgical treatment of DDD using implants.
	Additional and high-quality RCTs of the success of TDR treatment are still necessary (especially focused on the ability of implants to maintain good results even long after surgery, long-term wear resistance, occurrence of very late complications).
	It is recommended to further optimise both the design of the TDRs themselves and the surgical techniques as well.
	The growing importance is obvious of the 3D scan - 3D model - 3D printing chain for the diagnostics, design and production of implants.
	The technologies used in the 3D scan - 3D model - 3D printing chain should be studied and developed intensively.
	The study of regenerative procedures using iPSC cells shall be of great importance for the future treatment of DDD, among other things.
	The development of Artificial Intelligence has great potential for the augmented design and in evaluating large volumes of data for evidence-based medicine.
	The most promising treatment method appears to be gene therapy, which, however, may probably not be expected in the routine, safe treatment of DDD for many years.
	It is important to pay greater attention to primary prevention, because it is clear that the best replacement for the patient is one that is not actually needed.

It can be stated that the majority of the authors of the selected articles concluded that TDR replacements in medium- and long-term studies and for carefully selected patients demonstrated the ability to effectively treat pain - especially for the treatment of a single segment in young patients, who did not suffer from severe facet joints degeneration, deformities, instabilities and osteopenia (Salzmann *et al.* 2017). For even better clinical results, some authors recommend further optimization of both the design of the replacements themselves and the surgical techniques as well (Cui *et al.* 2018).

In terms of a comparison of the results of movable replacements with fusion methods, the conclusions of the authors were less unambiguous, with them more often leaning towards the finding that TDRs proved rather only their equivalency (Park 2015, Beatty 2018, Cui *et al.* 2018). However, to determine whether they are superior to fusion techniques, the authors recommend more high-quality RCTs. Some authors also mentioned results in which motion-sparing TDRs showed better success than fusion methods only in a short time after surgery, but after a longer period (5 years) the outcome was similar (Bai *et al.* 2019). Although complications and necessary reoperations of TDR were in the selected articles often reported to be less frequent than in fusion methods (e.g. 3.7 % to 11.4 % for TDR compared to 5.4 % to 26.1 % for the fusion method in Zigler *et al.* 2018), if a motion sparing TDR device fails, it is removed and a fusion operation in the given segment is usually performed (Pimenta *et al.* 2018). However, reoperation of TDR is considered to be complicated, risky and with uncertain results in terms of pain relief even with the successful achievement of subsequent fusion (Salzmann *et al.* 2017).

Based on the results of the studies, some authors believe that while an increased risk of developing ASD in the case of a fusion treatment has been clearly demonstrated (Beatty, 2018), the superiority of motion preserving replacements over fusions in reducing or preventing ASD has not been demonstrated and requires further monitoring and evaluation (Park 2015). In addition to classic TDR using the "ball and socket" conception for achieving motion using metal alloys and polymers, there are now new generations of implants which contain a technical element which allows viscoelastic deformation, and thereby a greater imitation of one of the important physiological functions of the intervertebral disc: the shock-absorbing ability (Büttner-Janz *et al.* 2014, Othman *et al.* 2019). For example, the M6-L (Orthofix Medical Inc., Lewisville, TX, USA) total disc replacement is a lumbar viscoelastic disc replacement that aims to mimic a physiologic intervertebral disc. M6-L received CE Mark Approval for implantation in the European Union and Australia in 2006 (Faulks *et al.* 2022). Faulks *et al.* (2022) described a series of sixty patients who had undrergone LTDR with the M6-L device. In this mid-sized single institution case series the M6-L demonstrated long-term effectiveness and durability and showed maintenance in motion up to 10 years. But nevertheless the authors concluded that further multi-center studies should be considered to assess the long-term efficacy.

In the selected articles it is stated that despite the initial promising success of DDD treatments with TDR, this method is not used on a large scale. For example, only 0.74% of surgical procedures performed for LDDD in the United States in 2019 were TDR (Upfill-Brown *et al.* 2022). The reasons given by the authors include the strict indications for their use, difficult surgical techniques with a long learning curve, a fear of late complications and difficult reoperations, as well as conflicting conclusions from studies, problems with reimbursement of this treatment or the distrust of conservative physicians in the new methods (Salzmann *et al.* 2017, Beatty 2018, Cui *et al.* 2018). The legitimate concerns of patients may also contribute to lower use, as in the case of LBP treatments due to DDD, the surgical option is relatively aggressive and while back pain is not a cause of death, invasive surgery and complications arising from it may become one (Park 2015).

It is also mentioned that with increasing age the rate of diagnosed degenerative changes in the spine increases in patients who do not suffer from LBP, which raises the question of to what extent can radiologically detected degenerative changes in elderly patients be the real cause of their low back pain (Park 2015, Mattei *et al.* 2017), even if a link between increasing age and the incidence of DDD is considered to exist (Beatty 2018, Pimenta *et al.* 2018, Othman *et al.* 2019).

Most authors concur that additional and high-quality RCTs of the success of TDR treatments are still necessary, not only to confirm previous findings in larger test groups but also to answer questions about the ability of implants to maintain good results even a long time after surgery, and to resist long-term wear and the occurrence of very late complications (Büttner-Janz *et al.* 2014, Park 2015, Park 2017, Cui *et al.* 2018, Pimenta *et al.* 2018, Wuertinger *et al.* 2018). For example, Faulks *et al.* (2022) indicates, that (also) heterotopic ossification and wear debris remains a long-term concern in spinal arthroplasty due to adverse effects on motion preservation and clinical outcomes. In addition to conflicting findings, which led some authors to believe that neither the noninferiority of TDR to fusion methods (Mattei *et al.* 2017) nor (all the more so) their superiority has been convincingly proven, the problem of implant manufacturers sponsoring certain studies was also pointed out, which, according to the authors, may bring some limitations in terms of the results (Park, 2015). Several authors of the selected articles thus conclude that fusion should (or will) remain the primary method of surgical treatments of DDD using implants for the time being (Park 2015, Salzmann *et al.* 2017).

Current trends, advanced methods and their results

Current surgical treatments of DDD are relatively aggressive, invasive and carry perioperative and postoperative risks. In addition, they do not treat the degeneration itself, but at best they try to replace the intervertebral disc with a motion preserving device. However, these usually do not offer any „higher“ function which a healthy disc normally provides (e.g. transport of fluid). Another negative effect occurs with quite invasive intervention into the surrounding structures of the complex and interconnected system during the implantation. In the selected articles, some studies determined that although surgical treatments provided faster pain relief to patients compared to conservatively treated cases, the results were basically the same after 1 year (Beatty, 2018). Not only for this reason, but also due to the fact that the field of medicine is affected by new technologies, bringing new possibilities, the following is a very brief overview of the methods of DDD treatment based on advanced procedures (especially 3D printing, regenerative medicine, including tissue engineering and gene therapy).

3D printing

The technology of 3D printing represents an ongoing technical revolution which affects many fields and is strongly associated with 3D computer models. According to the selected articles, 3D printing was used in the field of spinal medicine for the first time in 1999 to print a model of the spine in order to visualize its complex deformities, and the first spinal, titanium, 3D printed implant appeared in 2009 (Gadia *et al.* 2018, Hsu *et al.* 2018).

Nowadays, 3D printing is increasingly being used in medicine wherever the individuality of the patient is important (anatomical models for planning surgery, guides, implants) and longer delivery times (currently approximately 5 to 6 weeks) and higher prices are not an issue (Hsu *et al.* 2018). Porous structures for tissue ingrowth or modification of the stiffness of the implant, which would not be possible to produce by conventional methods, appear. The application of 3D printing is also studied in tissue engineering, in which the printing takes place using special so-called “bioinks”, containing cells, including stem cells. The ultimate goal of this “bioprinting” is apparently to build tissues and whole new organs for transplantation (Gadia *et al.* 2018, Sharma & Goel 2018). In this way, the first intervertebral discs were experimentally printed (Gadia *et al.* 2018). These replacements were implanted successfully in animal models, e.g. rodent tails (Moriguchi *et al.* 2017), but there is still a long way to go from these promising results to clinical success in humans. Currently, methods of so-called “4D” printing, 3D printing at nanoscale (so far very slow), or faster, volumetric 3D printing using holograms are also being studied.

A separate chapter is the use of artificial intelligence (AI), which is discussed in this context when it is incorporated into the chain of so-called “augmented design” (designs of solutions based on tasks provided by humans and his or her supervision of the whole process). As can be seen, even from the examples of the current use of AI-based tools, such as ChatGPT (a chatbot developed by the OpenAI laboratory) or, for example, Midjourney (a program that generates images from natural language descriptions, developed by Midjourney, Inc.), the potential of AI-based augmented design seems to be very high.

Cell therapies and tissue engineering

These procedures are part of the so-called “regenerative medicine” and aim at regenerating or even replacing tissues so that their original or natural function is restored or achieved (Sampogna *et al.* 2015). Cell therapies work with the injection of cells (or growth factors), tissue engineering with so-called “scaffolds”, which are special structures mostly seeded with cells, aimed at gradually replacing specific tissue.

Due to their naturally regenerative function even in the organisms themselves, stem cells are used in these procedures. Among them, in addition to the often-mentioned mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs) represent a very significant type (Goldberg *et al.* 2017). These are created by special methods from common cells obtained from the body of an adult. However, the use of stem cells at the current stage of development poses a risk of developing undesirable cancer growths (Saeed *et al.* 2016).

In the case of the relatively promising results from animal models, the problem of transmission - the achievement of the same successes in humans, is mentioned (Moriguchi *et al.* 2017).

According to van Uden *et al.* (2017), the interconnection of spinal structures is overlooked – it is not possible to solve the degeneration of only one part (disc) and ignore the other (e.g. endplates).

The potential of regenerative methods is, therefore, seen mainly in patients with mild to moderate DDD without significant biomechanical changes in the affected spinal segment.

However, the current unsatisfactory understanding of both the complex processes taking place in the tissues and the source of the pain itself was sometimes highlighted in the selected articles, as well as the fact that in some studies considerable results were achieved even with the use of the placebo effect only (Serhan, 2018). Thus the authors conclude their findings by recommending other, high-quality, double-blinded RCTs. Therefore, it may be stated that these methods of treatment are in their infancy.

Gene therapy

Genes are basic units of genetic information which are essential for the form, growth, properties, life, and reproduction of all known organisms – so it is not surprising that theories about a link between genes and diseases have emerged, not least in congenital diseases (Kc & Steer, 2019). According to some researchers, the origin of DDD also contains a strong genetic component to which age, environmental factors, as well as the method and degree of physical loading of the spine contribute (Taher *et al.* 2012, Karaarslan *et al.* 2017). However, there are also authors who did not see genetic factors in connection with DDD (Karaarslan *et al.* 2017).

From the selected articles, it is clear that the fundamental technical problem so far is the delivery of the therapeutic gene to the target cells with the necessary efficiency and with minimal risks for the patient - the choice of a suitable “vector”. The link between the performance of the vector and its toxicological profile is pointed out, which so far means that with increasing efficiency of the vector, its toxicity also increases and vice versa (Ramamoorth & Narvekar 2015). The efficiency is relatively high with viral vectors compared to non-viral methods, but the main drawbacks of using viral vectors are its cytotoxicity, immunogenic toxicity and the risk of insertional oncogenesis (Ramamoorth & Narvekar 2015, Uddin *et al.* 2020).

New methods, such as CRISPR technology, bring new possibilities but also new challenges (Uddin *et al.* 2020).

Although some promising results have been achieved in research of treatment (including DDD), it is again justified to state that this method of treatment is still in its infancy.

Prevention

During the literature search, only 1 article was found dealing with the topic of prevention. The authors note in the introduction that despite a number of scientific publications and studies on the treatment of back pain, work on prevention, especially the primary incidence of pain, is not very common.

Regarding the prevention of secondary back pain, the authors found that from a number of frequently mentioned measures such as exercises, education, ergonomics in the workplace, advice on how to lift loads or special aids for lifting objects, mattresses, waist belts, or shoe insoles, the most effective measures are exercises, or exercises complemented with education. However, even for these findings, according to the authors, the results of the studies do not have a firm evidence base, and therefore they recommend the performance of other, high-quality studies which would address effective and realistically applicable prevention strategies and confirm their effectiveness on a larger scale. The authors also pointed out that health care reimbursement systems in practice can be sometimes focused more on the quantity of the treatment rather than on its quality. In the case of media campaigns, the authors mention focusing on recommending specific behavior rather than changes in beliefs and attitudes, as well as the incorporation of new ways of disseminating information, such as social networks. Otherwise, the authors focus mainly on the overall management of the treatment of low back pain, in which they emphasize the implementation of the best practice known (Foster *et al.* 2018).

Evaluation of the current state of DDD treatments using intervertebral disc replacements

One of the differences between fusion implants and TDR is based on the treatment conception itself. While after fusion is achieved, the task of the corresponding implant is fulfilled, motion-preserving replacements should remain functional throughout the whole lifespan of the implantation. The failure of TDR (loosening and migration, breakage, etc.) often leads to reoperation, and this, in the area of the spine, represents a more difficult and risky procedure than, for example, the reoperation of the knee joint replacement. In addition, the risk logically increases with the patient's age. Therefore, if a mean age of patients surgicaly treated with TDR of 45 years was mentioned in the Review section, then these implants should ideally be able to last up to at least 30 years without failure, or their failure should lead to spontaneous fusion without the need for reoperation. However, information on such a long-term survival of these implants is not yet available, even though they were introduced just 30 years ago. One of the reasons for this may be that new models are constantly appearing often with different designs, and the timeline for achieving truly long-term results for the types available on the market is, therefore, still being shifted to later. In relation to this is the question of how reasonable it is to evaluate motion-preserving replacements, which have a significantly different conception of achieving movement (e.g. "ball and socket" compared to newer replacements with a deformable, shock-absorbing element) and the results achieved with them, together as the results of this type of replacements in general, regardless of their specific design. The relevance of the results may also be influenced by the fact that they are not measured directly but only on the basis of the subjective answers of patients in questionnaires.

Due to the absence of information on the truly long-term results of specific TDRs, resulting in insufficient knowledge of very late complications and their negative potential, and also due to several other reasons mentioned – for example the pressure on strict indications for TDRs to ensure the best possible outcomes or fusion surgery as a common solution to failed TDR, it is understandable that many spinal surgeons even today are still more inclined to fusion as to the gold standard of operative DDD treatments using implants.

In younger patients with LBP, the relevant question is whether the potential of conservative treatment is sufficiently used in practice and according to the selected articles there still appears to be a room for improvement in this field.

However, the fact cannot be ignored that the development of, for example, hip replacements, which are currently considered to be handled quite well, has been ongoing for approximately 60 years and these replacements and their implantation techniques are still being developed. Motion sparing disc replacements have been under development for approximately 30 years and it can definitely be said that the task of developing effective TDR is more difficult due to the complexity of the spinal system.

Despite its importance, it seems (from the article search results) that the prevention of DDD, and thereby also LBP, is relatively neglected.

Future perspectives

The question of future development is always about what should and what will actually happen. Due to random phenomena, the value of predicting what will actually happen is, of course, debatable. Therefore, in this section considerations will focus primarily on what seems (in our opinion) favourable to happen in this field.

Regenerative medicine and especially gene therapy have great potential and should, therefore, be given sufficient attention. The use of iPSC seems to be very interesting for regenerative treatment, and mastering gene therapy seems in general to be a kind of a „holy grail" of medicine. However, as long as these procedures have greater than a low risk of serious side effects, it obviously should not be used more commonly for this treatment, especially in patients with less severe forms of DDD. The success of tissue-engineered disc replacements implanted in more advanced stages of DDD will probably always be negatively affected by the advanced degeneration of associated tissues on which the proper function of the replacement will depend. Therefore, methods of conservative treatment with determining and ensuring the effectiveness of various approaches as a part of evidence-based medicine should certainly have their place in the future as well. Emerging technologies for processing large volumes of data (information on the results of various treatment procedures), including projects containing an element of artificial intelligence, may be used to facilitate the selection of the most appropriate type of treatment. Artificial intelligence may also be used in the research and development of implants in the framework of augmented design, in which an increase in the importance of the 3D scan – 3D model – 3D printing chain with a focus on improving 3D scanning and 3D printing of smaller and more complex structures, for example, for tissue engineering may be expected. However, the safe, effective, and routine use of the mentioned methods of regenerative and gene treatment of DDD and others may be expected more in the distant future. All the more so as current spinal specialists sometimes have problems determining even the source of the pain itself in the complex and interconnected system of the spine, while the treatment of DDD will furthemore require the identification of the problem-relevant genes. \

Both fusion and motion sparing TDRs (more probably closer to the physiological pattern, with the possibility of shock absorption etc.) are expected to remain in practice for some time to come. In their further development, emphasis should be placed on mini-invasiveness, in which 4D printing may also bring new possibilities.

Mini-invasiveness is also significantly related to the whole area of imaging methods, which are currently dominated by CT and MRI. Imaging methods, essential for diagnostics throughout medicine, should be applied with the technologies which place a minimal burden on the patient (e.g. with X-ray exposure) while ensuring sufficient resolution for the subsequent creation of 3D models and 3D printing. Here, the aim is apparently to print the whole new organs using bioinks, containing suitable cells, maybe even on the basis of a preventive scan from the period when the patient was healthy.

For children and adolescents, the research and application of primary prevention should take place. Some influences, however, do not need to be studied as much: e.g. a healthy lifestyle, sufficient exercise and muscle strengthening, moderate and healthy eating, good quality shoes, chairs, beds, avoiding overloading the back, less stress and a greater feeling of happiness in life certainly support prevention. A special area of prevention research associated with gene therapy should be the study of the genes (but also, for example a lifestyle) of older people who do not suffer from DDD, even when their spines show degenerative changes. However, this is long-term research, and the question is to what extent today's society, which seems to be focused on financial gain, consumption, a hectic pace of life, etc., is capable of accepting such an approach which favors the suitable prevention over the treatment of consequences. Therefore, prevention of DDD should probably include the cultivation not only of the body but also of the spirit of each individual and thus of society as a whole.

LIMITATIONS

The presented results may have been distorted to a certain extent due to the selection of the articles being governed by the requirement that their full text has to be directly available at the time of searching in the given database. A university approach was also used when searching for articles in the databases and at least an abstract of all articles considered was available to the authors.

Due to the relatively wide range of topics, the chosen scope of this article may be too brief. The authors believe that this is the price for a comprehensive view while maintaining a reasonable scope of the article. In the event that there is a more detailed interest from the reader in a specific area, we therefore recommend the listed references.

A different perspective that is rather the R&D point of view, which is derived from the composition of the author's team, may differ from the common view of physicians and surgeons. On the other hand, this perspective brings the possibility of unusual insights and therefore also inspiration.

CONCLUSIONS

Considering the described findings, it is understandable that fusion remains the gold standard for the surgical treatment of DDD using implants, and intervertebral disc replacements are less widespread and used. It is recommended to further optimise both the design of the TDR itself and the surgical techniques as well. Additional and high-quality RCTs of the success of TDR treatment are still necessary, especially focused on the ability of implants to maintain good results even long after surgery, and to resist long-term wear and the occurrence of very late complications.

In terms of the advanced methods of surgical treatment, the growing importance is obvious of the 3D scan - 3D model - 3D printing chain for the diagnostics, design and production of implants. Consequently, the technologies used in this chain should be studied and developed with a great effort, in particular imaging and scanning methods (of adequate quality and also with a sufficient degree of patient safety) and also 3D printing methods, including micro- and nano-scales. Apparently, the study of regenerative procedures using iPSC cells (e.g. for the production of bioinks for 3D tissue printing) shall be of great importance for the future treatment of DDD, among other things. The development of artificial intelligence has great potential for the augmented design and in evaluating large volumes of data, which is also important for evidence-based medicine.

The most promising treatment method appears to be gene therapy, which, however, may not be expected in routine, safe treatment of DDD probably for many years. Not only for this reason, it is important to pay greater attention to primary prevention, because it is clear that the best replacement for the patient is one that is not actually needed.

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