The use of polymethylmethacrylate in cervical spine surgery

M Topalovic¹, S Kropenstedt², M Cabraja*¹

Abstract

Introduction
The use of polymethylmethacrylate (PMMA) after anterior cervical discectomy (ACD) shows high rates of graft migration and pseudarthrosis when compared with various other fusion procedures. Due to this fact, it is currently not considered the preferred choice of treatment in many countries. This review discusses the use of PMMA in cervical spine surgery.

Materials and methods
A literature review was conducted, and the articles were assessed for level of bias using the criteria recommended by the Cochrane Back Review Group.

Results
During last 30 years, five prospective and seven retrospective studies have been published that investigate PMMA-assisted ACD. While the radiological analysis shows inferior radiological results, the clinical outcome is not affected adversely by the intervertebral insertion of PMMA when compared with other replacement substrates.

Conclusion
Since there is no evidence that fusion is mandatory for clinical success, and no study has shown an inferior clinical outcome of PMMA-assisted ACD in comparison with other substrates, PMMA can be used successfully in cervical spine surgery. Furthermore, the level of bias of the published studies supports the need of a controlled randomized multicentre trial. Only if fusion is mandatory for clinical success in certain cases, alternative grafts should be preferred since PMMA produces inferior radiological outcomes compared to cages or bone grafts.

Introduction
Anterior cervical discectomy and fusion (ACDF) represents the golden standard in surgical treatment of degenerative disc disease (DDD)¹-³. Nevertheless, there is an ongoing discussion as to which fusion substrate provides the best clinical and radiological outcome. Autologous iliac bone crest, allograft bone, titanium, polyetheretherketone (PEEK) or carbon cages are widely used graft materials⁴. Recently, artificial discs have gained wide acceptance in the surgery of DDD⁵-⁸.

Polymethylmethacrylate (PMMA) is another replacement substitute for removed discs after anterior cervical discectomy (ACD) that was established in 1967 for cervical spine surgery⁹.

The first application of a polymerizing material for medical purposes dates back to 1941, when it was used to cover calvarial defects¹⁰. Years later PMMA was used as a prosthesis of the femur head, which was a further step to establish PMMA in clinical procedures¹¹. Today PMMA is considered the gold standard for screw-augmentation in spine surgery¹²-¹⁹ and for vertebroplasty/kyphoplasty²⁰-²¹. As there have been reports of higher rates of graft migration and pseudarthrosis as well as of unsatisfying results in restoring disc height and sagittal alignment for PMMA in cervical spine surgery¹²-²⁷, spine centres in many countries have stopped using it as an intervertebral disc replacement material. PMMA-assisted ACD nonetheless provides good clinical outcomes compared with other substrates¹,²⁴,²⁶-²⁸, and is an economical alternative to titanium and PEEK implants. Also the successful application of artificial discs that preserve the segmental motion strongly indicates that a fusion of cervical segments is not mandatory for clinical success⁵-⁸. For these reasons PMMA is, for example, still used in Germany²⁵,²⁹-³¹.

The objective of the review was to report the clinical and radiological results of PMMA-assisted ACD with the focus on patients’ safety and complications. Furthermore, the existing literature was to be assessed for level of bias²⁹.

Materials and methods
A computer-aided research through related literature was conducted by the authors independently. Search terms that were used to find relevant articles in the MEDLINE and EMBASE databases were: ‘Polymethylmethacrylate’, ‘PMMA’, ‘bone cement’, ‘cervical spine surgery’, ‘ACD’, ‘PMMA-assisted ACD’, ‘PMMA-assisted ACD’ and ‘PMMA-assisted ACD’.

The articles were assessed by the authors for level of bias using the 12 criteria recommended by the Cochrane Back Review Group. Studies with a high risk of bias were defined as having met fewer than 6 of the 12 criteria, whereas low risk of bias was having met 6 or more criteria³². As only few studies on the...
reported subject exist, retrospective studies were included in the review as well.

Results
Five prospective and seven retrospective studies that investigated the outcome of PMMA-assisted ACD have been published over the last 30 years. The results of yet another retrospective study were presented during the 63rd DGNC in 2012 in Leipzig, Germany. These 11 studies have been assessed for level of bias using the 12 criteria recommended by the Cochrane Back Review Group (see Table 1).

Clinical outcomes
The first prospective randomized trial was performed by van den Bent et al. and published in 1996. The investigational group consisted of 42 patients who received PMMA after ACD, with the control group’s 39 patients being treated by microdiscectomy only (MDO). The aim of the study was to assess if PMMA improves the outcome of patients undergoing discectomy with regard to neck pain. The study endpoint was the assessment of the clinical outcome 2 years after surgery.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Study design, follow-up</th>
<th>Groups</th>
<th>No. of patients</th>
<th>Clinical outcome</th>
<th>Fusion (according to author)</th>
<th>Re-OP</th>
<th>Level of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roosen, 198226</td>
<td>Retrospective 1-10 years</td>
<td>Trauma DDD Myelopathy</td>
<td>90 156 75</td>
<td>63.3% compl. recovery 73.5% exc. or good 45.2% exc. or good</td>
<td>N/A N/A</td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>Böker et al., 198917</td>
<td>Retrospective 15-20 years</td>
<td>PMMA</td>
<td>57</td>
<td>Not assessed</td>
<td>89% 0</td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>Samii et al., 198918</td>
<td>Retrospective 4.8 years</td>
<td>PMMA</td>
<td>438</td>
<td>81% pain relief</td>
<td>Not assessed 35 (8 %)</td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>van den Bent et al., 199626</td>
<td>Prospective 2 years</td>
<td>PMMA MDO</td>
<td>42 39</td>
<td>70% good 77% good</td>
<td>28% 63% 0</td>
<td>Low risk</td>
<td></td>
</tr>
<tr>
<td>Hamburger et al., 200127</td>
<td>Retrospective 12.2 years</td>
<td>PMMA</td>
<td>249</td>
<td>77.5% exc. or good</td>
<td>53.8% 24 (9.6 %)</td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>Jöllenbeck et al., 200130</td>
<td>Prospective 7 days</td>
<td>PMMA TTC</td>
<td>100 100</td>
<td>81% compl. recovery 78% “</td>
<td>Not assessed 1 (1 %) 1 (1 %)</td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>Bárolocher et al., 20023</td>
<td>Prospective 1 year</td>
<td>MDO ABG PMMA TTC</td>
<td>33 30 26 36</td>
<td>75.5% exc. or good 80% “ 87.5% “ 94.4% “</td>
<td>93.3% 65.3% 0 97.2% 2 (6.1 %) 1 (3.3 %) 0 0</td>
<td>Low risk</td>
<td></td>
</tr>
<tr>
<td>Chen et al., 200534</td>
<td>Prospective 2 years</td>
<td>PMMA cage</td>
<td>63</td>
<td>100% exc. or good</td>
<td>100% 0</td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>Korinth et al., 200628</td>
<td>Retrospective 6 years</td>
<td>PMMA</td>
<td>124</td>
<td>93.6% exc. or good</td>
<td>Not assessed 3 (2.4 %)</td>
<td>High risk</td>
<td></td>
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<tr>
<td>Schröder et al., 200724</td>
<td>Prospective 2 years</td>
<td>PMMA TTC</td>
<td>53 54</td>
<td>85% exc. or good 77.7% “</td>
<td>66% 0</td>
<td>Low risk</td>
<td></td>
</tr>
<tr>
<td>Mudo et al., 200940</td>
<td>Retrospective 2 years</td>
<td>PMMA</td>
<td>46</td>
<td>&gt; 69% exc. or good</td>
<td>52% N/A</td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>Cabraja et al., 201139</td>
<td>Retrospective 8.1 years</td>
<td>PMMA</td>
<td>50</td>
<td>66% exc. or good</td>
<td>66% 0</td>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>Klingler et al., 201231</td>
<td>Retrospective 2.5 years</td>
<td>PMMA PEEK cages</td>
<td>70 39</td>
<td>No difference</td>
<td>51% 65% 2 (2.9 %) 1 (2.6 %)</td>
<td>High risk</td>
<td></td>
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clinical differences between both groups could be found. While neck pain disappeared earlier in patients with PMMA insertion, the difference was no longer visible after 1 year. Jöllenbeck et al. published a prospective, non-randomized study in 2001 that compared PMMA with titanium cages in 200 patients (100 patients in each group)\textsuperscript{30}. Again, the clinical outcome did not differ between both groups, and about 80% of all patients reported a complete recovery of their pre-operative symptoms. Due to the short follow-up of only 7 days, an assessment of bony fusion was not performed. Bärlocher et al. published a prospective randomized study of 125 patients in 2002\textsuperscript{1}. The aim of the study was to evaluate whether patients benefit more from insertion of PMMA, a titanium cage or an autologous bone graft (ABG) than from MDO. The patients were randomized into four groups and followed for 1 year. There was no significant difference in clinical outcome between PMMA and the other groups. The authors concluded that titanium cages provide several advantages compared to ABG-insertion and MDO. PMMA was judged to be a good alternative to cage-assisted surgery but was criticized for its lack of immediate fusion. Schröder et al. performed a prospective randomized trial comparing titanium cages and PMMA filling after ACD\textsuperscript{24}. The primary endpoint was the clinical outcome after 2 years. 85% of the PMMA group and almost 78% of the titanium group reported a successful surgery after 2 years. The clinical outcome did not differ between the groups. Time of surgery was reduced by the application of titanium cages (14 min mean). Chen and colleagues evaluated patients that underwent ACD with insertion of a filled PMMA cage in a prospective study\textsuperscript{26}. The round, hollow cage (Osteobond, Zimmer, Warsaw, IN) had been designed to provide a better fusion than the known PMMA inlays and had proved to provide sufficient strength for clinical application in a biomechanical analysis\textsuperscript{35}. The cages were filled with autologous bone graft that supported the fusion. All of the 63 patients reported a favourable clinical outcome. Roosen published a study about his experimental and clinical experience with PMMA in 1982\textsuperscript{26}. The clinical study population consisted of 321 patients who had received an intervertebral PMMA filling after ACD. 90 patients were operated on due to a trauma, 182 suffered from DDD with radicular pain and neck pain, and 75 patients had been diagnosed with cervical myelopathy. The trauma patients improved in a large number of cases, mainly depending on preoperative status. 73.5% of the patients suffering from radicular symptoms and neck pain showed an excellent or good outcome. 45.2% of the patients with a cervical myelopathy reported a favourable outcome. Böker et al. conducted a retrospective study that focused on the radiological outcome of patients after PMMA-assisted ACD\textsuperscript{37}. The study of Samii et al. focused on the clinical outcome of 438 patients after ACD and PMMA insertion and did not demonstrate any radiological data after surgery\textsuperscript{38}. The patient population suffered from radiculopathy and myelopathy due to DDD. More than 80% of patients experienced substantial pain relief and improvement of motoric symptoms. More than 66% of patients suffering from cervical myelopathy reported substantial relief of symptoms. Hamburger et al. conducted a long-term evaluation after ACD and PMMA insertion in 249 patients\textsuperscript{27}. The authors not only acknowledged other surgeons’ findings that PMMA produces less bony fusion than other materials but also pointed out that the necessity for fusion is controversial and has not been proven scientifically yet\textsuperscript{31}. They performed the study to report their own experience with PMMA-assisted ACD. 77.5% of their patients reported a favourable clinical outcome 10 to 15 years after surgery. 18.9% of the patients experienced at least a fair outcome. Korinth et al. published a retrospective and non-randomized follow-up study of 292 patients\textsuperscript{29}. 124 of these patients underwent a monosegmental ACD with PMMA insertion, and 168 patients were treated with a posterior foraminotomy. The patients of the PMMA group showed a significantly better clinical outcome than the patients after posterior foraminotomy (93.6% versus 85.1%). Radiological parameters were not evaluated. The indication for anterior surgery differed from that for posterior surgery, which was acknowledged and discussed by the authors as a potential selection bias of the study. Cabrera et al. presented a retrospective long-term follow-up study of 50 patients\textsuperscript{30}. The aim of the study was to evaluate whether the preserved motion of a pseudarthrotical segment might have a positive influence on the development of an adjacent segment disease. No clinical differences could be found between patients with pseudarthrosis and solid arthrodesis of the operated level. 66% of the patients reported a favourable clinical long-term outcome. Mudo et al. compared patients with radiculopathy and myelopathy after PMMA-assisted ACD and focussed on the impact of cervical alignment on clinical outcome. 69% (35 patients) of the patients suffering from cervical myelopathy reported a favourable clinical outcome. 89% (10 patients) of the patients suffering from radiculopathy stated a favourable outcome as well\textsuperscript{31}. Klingler et al. presented their retrospective study during the 63rd DGNC in 2012 in Leipzig, Germany\textsuperscript{31}. The authors compared three groups of patients, 109 patients in total, who either underwent ACD with implantation of cervical PEEK cage (39 patients), ACD with Sulfix\textsuperscript{®}. PMMA implantation (38 patients) or ACD with Palacos\textsuperscript{®}-PMMA insertion (32 patients). The clinical outcome
after a mean of 2.5 years assessed by the neck disability index (NDI) significantly favoured the cage group compared to the Sulfix®-PMMA group, but not compared to the Palacos®-PMMA group. Comparison of the cages with both types of PMMA revealed no differences regarding clinical outcome. Assessment of pain and SF-36 component summaries did not reveal any statistical differences between the three groups.

Radiological outcomes
The radiological results regarding fusion by van den Bent et al. were in favour of the control group, since only 28% of the patients treated with PMMA showed fusion according to the author’s criteria: bone bridging and absence of movement in functional X-rays. Patients with a bony union showed a slightly better clinical result than patients without union in both groups. Bärlocher et al.’s radiological analysis showed that a fusion of the segment did not occur at all in the PMMA group. The radiological analysis by Schröder et al. revealed a significantly higher rate of fusion when titanium had been used (87% versus 66%). Fusion was deemed unimportant for a favourable clinical outcome. The radiological analysis by Chen and colleagues revealed a fusion in 100% of the cases. The cage was deemed safe for further clinical application. Roosen reported bony incorporation of the PMMA requiring up to 2 years, but did not give any specific data about the bony fusion. Complete radiological data could only be assessed for 39 patients. Böker et al. conducted a retrospective study that focused on the radiological outcome of patients after PMMA-assisted ACD. The aim of the study was to investigate potential long-term risks that were thought to be connected to PMMA insertion: damage to nerve structures due to the thermic reaction during PMMA polymerization, pseudarthrosis and segmental instability, development of a malignoma. X-rays were available from 57 patients 10 to 15 years after surgery. A ‘maximal’ bone engraftment was found in 51 cases (89%) and for 55 patients (96%) the segment was rated as fused using a semiquantitative analysis of the bone formation around the PMMA graft. No malignoma was detected in the comparably small patient collective. Clinical data were not assessed. The authors concluded that the supposed disadvantages of PMMA such as development of a malignoma and risk of instability were not supported by their data. Radiological data by Hamburger et al. was obtained for 84 patients. Images taken at least 2 years after surgery were only available for 39 patients. Fusion around the dowel was observed in 53.8% of these cases. In 15 of 39 patients (38.5%), no fusion could be seen. By Klingler et al. fusion was achieved in 65% of the cage group and in 57% and 45%, respectively, of the two PMMA groups. Mudo et al. reported successful fusion in 52% of their patients, but found a strong correlation of a lordotic alignment with clinical success, while fusion did not have any impact on clinical success.

Complications
Subsidence of the PMMA graft was observed in 23% of cases, causing van den Bent et al. not to recommend the application of PMMA in cervical spine surgery. It has to be noted, though: the existence of neck pain after ‘discectomy only’ was related to the absence of a proper disc substitute leading to pain-inducing anatomical conditions, but the authors did not mention that neck pain is a common condition of DDD. Furthermore, the authors acknowledged that the relevance of fusion for clinical success is unclear and recommended the use of PMMA only for those surgeons who do not consider fusion a critical condition for clinical success. Jöllenbeck et al. found that the titanium cages subsided more frequently into the adjacent vertebral bodies than the PMMA implants. Graft breakage and graft displacement were found more often in the PMMA group but this did not result in more revision surgery than in the titanium group. Revision surgery was required only once in each group. It is noteworthy that Bärlocher et al. showed that the rate of segmental subsidence was lowest in the titanium and the PMMA group, the maintenance of intervertebral height being regarded as the main reason for a lower incidence of radicular pain after 1 year compared to the ABG and MDO group. Roosen reported a 5% rate of surgery-related complications. In 15.3% of the trauma cases, a PMMA dislocation was observed, though it is unclear if these patients required or received revision surgery. Roosen concluded that PMMA appears to be an equivalent alternative for intervertebral fusion spacers. Samii et al. reported that reoperation was necessary in 35 cases (8%), but in only 6 cases due to dislocation of the PMMA graft. Hamburger et al. reported that repeat surgery was necessary in 9.6% of cases because of persisting or recurring pain and/or neurological symptoms or because of symptoms due to changes in adjacent levels. No revision surgery was required because of an implant dislocation. A displacement of the PMMA inlay was detected in 8 of 75 patients (10.7%) but did not require surgical revision. The authors deemed PMMA-assisted interbody fusion after ACD as a safe and reliable surgical method with a long-term outcome that is comparable with other procedures discussed in the literature. Korinth et al. showed that 3 patients of the PMMA group and 12 patients of the posterior group had to undergo repeat surgery. Cabraja et al. showed a high rate of pseudarthrosis in patients undergoing PMMA-assisted ACD (34%). Signs of an adjacent level disease could be seen more often in the group of patients with

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solid arthrodesis, but the appearance of ASD correlated more with a patient's age than with the movement of the operated segment\textsuperscript{39}. Cage-substance and loss of correction found by Klingler et al.\textsuperscript{31} was highest in the cage group. Revision surgery for dislocated implants was required in one case from the cage-group and two cases from the Palacos\textsuperscript{®}-PMMA group. Mudo et al. described a complication in 12 cases of the myelopathy group, including two patients who died. The two fatal complications did not appear to be graft related. A graft dislocation was described in 3 of 46 patients, but the authors did not state if any revision surgery was required\textsuperscript{40}.

**Discussion**

The authors have referenced some of their own studies in this review. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964) and the protocols of these studies have been approved by the relevant ethics committees related to the institution in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in these studies.

All available studies on PMMA-assisted ACD that assessed the clinical results of their patients reported a favourable outcome of the PMMA patients that is comparable to even most advanced alternative procedures\textsuperscript{41–46}. Most of the PMMA studies report an inferior outcome with regard to bony fusion, but this apparently has no influence on the clinical outcome and patient satisfaction. In general, subsidence of interbody grafts consisting of titanium or PEEK is currently acknowledged as a possible complication of ACD\textsuperscript{46–50}. The risk of secondary surgical procedures using PMMA implants after ACD appears to be the same as to these alternative procedures\textsuperscript{41,44,51}.

The study designs of the few available publications show certain limitations based on either their retrospective character and/or monocentric evaluations of a comparatively small patient collective and sometimes limited observational period. As is the case with many other grafts, which are currently used in spine surgery, there are no studies with an evidence level 1 to assess the deployability of PMMA. Thus, even the widely accepted opinion on PM-MA’s lesser capacity to produce fusion lacks profound evidence\textsuperscript{52}. There is even less evidence that fused patients have a better clinical outcome than non-fused patients. The successful application of artificial discs that maintain or restore the mobility of operated segments supports the assumption that fusion and clinical success are independent factors in at least the surgery of DDD\textsuperscript{41,44,51}. The use of PMMA as an intervertebral substrate was therefore advocated in Germany for decades and inserted in thousands of patients\textsuperscript{53}.

The review included data from two databases, but according to the Cochrane Back Group MEDLINE and EMBASE represent sufficient literature sources due to small overlaps of these databases\textsuperscript{52}. The review did not include literature that is not written in English and thus, does not offer an overall literature review. The recommendation of the Cochrane Back Group to review randomized-controlled trials (RCTs) was not met due to the small number of RCTs on this subject. Thus, we searched all available studies on PMMA as an intervertebral disc spacer.

**Conclusion**

PMMA-assisted ACD provides comparably good clinical outcomes compared with other substrates and is an economical alternative to other implants. There are few materials in cervical surgery that have as long a history in use for medical purposes. Although PEEK or titanium cages can be handled in an easier manner intraoperatively, for all of the mentioned reasons, PMMA is still chosen after ACD in a number of German clinics. The high risk of bias of the published studies on PMMA after ACD supports the need of a multicentric controlled randomized trial to assess the deployability of PMMA in cervical spine surgery. Only if fusion is mandatory for clinical success in certain cases, alternative grafts should be preferred since it appears to produce inferior radiological outcomes compared to cages or bone grafts.

**Competing interests**

Dr. Cabraja is an expert in a current litigation dealing with the applicability of PMMA in spine surgery.

Dr. Kroppenstedt is a consultant of B Braun Aesculap, Tuttinglen, Germany.

**Abbreviations list**


**Acknowledgement**

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**References**


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