



1

The Risks of Polymethyl Methacrylate: An Integrative Review of 587 Complication Reports

Os riscos do polimetilmetacrilato: Revisão integrativa de 587 casos de complicações

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Abstract

Introduction The demand for minimally-invasive esthetic procedures has boosted the use of polymethyl methacrylate (PMMA) as a dermal filler, which was initially approved for human immunodeficiency virus (HIV)-related lipodystrophies. Improper PMMA use can lead to severe complications, including inflammation, material migration, infections, and systemic repercussions. The present review investigated PMMA-related risks and complications reported in the literature over the past 20 years.

Materials and Methods We conducted an integrative review of descriptive studies on PMMA complications published from 2004 to 2024 and retrieved from PubMed, Scientific Electronic Library Online (SciELO), and Scopus. We analyzed 38 studies, encompassing 587 cases, and excluded articles published outside the specified period and those not meeting the inclusion criteria.

Results We identified 587 cases of PMMA-related complications, 64% of them occurring in Brazil. The most common complication site was the malar region, followed by the nasolabial fold, the gluteal area, and the lips. The complications ranged from immediate to delayed, and from mild to severe. The most frequent complications included erythema (26%), pruritus (16%), edema (11%), granulomas (21%), nodules (14%), and skin changes (8%). Severe cases included renal failure, hypercalcemia, septic shock, infections, and tissue necrosis. The volume injected ranged from 1.9 to 900 mL. The treatment predominantly involved steroids, antibiotics, and surgical interventions, including excisions, abscess drainage, and debridement.

Conclusion The use of PMMA fillers may lead to severe complications, often unrelated to the correction of HIV-related lipodystrophies; PMMA presents significant risks, including systemic complications, requiring surgical removal.

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Keywords

review

► risk

► case reports

dermal fillers

polymethyl

methacrylate

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Resumo	Introdução A demanda por procedimentos estéticos minimamente invasivos impul-	
	sionou o uso do polimetilmetacrilato (PMMA) como preenchimento dérmico, que a	
	princípio foi aprovado para lipodistrofias relacionadas ao vírus da imunodeficiência	
	humana (HIV – human immunodeficiency virus, em inglês). Seu uso inadequado causa	
	graves complicações, como inflamações, migração do material, infecções e repercus-	
sões sistêmicas. Nesta revisão, objetivamos realizar uma investigação sobr		
	riscos e complicações relatadas na literatura nos últimos 20 anos.	

Materiais e Métodos Realizamos uma revisão integrativa de estudos descritivos sobre complicações do PMMA publicados entre 2004 e 2024, utilizando as bases de dados PubMed, Scientific Electronic Library Online (SciELO) e Scopus. Foram analisados 38 estudos, totalizando 587 casos, e foram excluídos artigos publicados fora do período analisado ou que não atendiam aos critérios de inclusão.

Resultados Encontramos 587 casos de complicações associadas ao PMMA, sendo que 64% deles ocorreram no Brasil. O sítio mais frequente foi a região malar, seguido do sulco nasogeniano, da região glútea, e dos lábios. As complicações variaram entre imediatas e tardias, e de repercussões simples a mais severas. As mais frequentes foram: eritema (26%), prurido (16%), edema (11%), granulomas (21%), nodulações (14%) e alterações cutâneas (8%), incluindo casos graves de insuficiência renal, hipercalcemia, choque séptico, infecções e necrose de tecido. A quantidade injetada de material variou de 1,9 a 900 mL, e, no que tange ao tratamento, houve predominância de esteroides, antibióticos e necessidade de abordagem cirúrgica, com realização de excisões, drenagem de abscesso e desbridamento.

Palavras-chave

- polimetilmetacrilato
- preenchedores dérmicos
- relatos de casos
- ► revisão
- ► risco

Conclusão Preenchimentos com PMMA estão associados a complicações graves, e seu uso muitas vezes não está relacionado à correção de lipodistrofias por HIV. O material tem riscos significativos, incluindo complicações sistêmicas, com a necessidade de remoção cirúrgica.

Introduction

The demand for minimally-invasive aesthetic procedures promising efficient, satisfactory results and a short recovery time has increased in recent years.¹ Cosmetic procedures, such as dermal fillers and facial and body volumizers, have emerged as popular alternatives to conventional plastic surgery, promising quick recovery and giving the false idea of fewer risks, meeting patients' expectations.²

In this context, polymethyl methacrylate (PMMA) is a widely used filler. It is a non-absorbable plastic component in spheres inserted into a vehicle to enable injectable application.³ The initial approval of PMMA for outpatient use in Brazil occurred in 2009 by the Ministry of Health for the treatment of lipodystrophies secondary to the adverse effects of antiretrovirals for HIV treatment.^{4,5} However, over the years, the indiscriminate and inappropriate use of PMMA has resulted in numerous immediate and delayed complications.³

Immediate PMMA complications include inflammatory reactions, pain, and infections shortly after the application. Such complications can range from minor adverse reactions, such as erythema and edema, to serious adverse effects, including tissue necrosis, ocular involvement, severe infections, and renal failure due to hypercalcemia.^{5–7} Acute complications can persist and evolve into granulomatous formations, recurrent infections, autoimmune diseases, and chronic renal failure. In addition, material migration to undesirable areas can result in local asymmetries and deformities many years after PMMA application.⁸

As a non-absorbable material, the interaction of PMMA with the adjacent tissue hinders its isolated removal. The irreversible nature of PMMA application is a major limitation.^{3,5,8} In the face of complications such as granulomas, chronic inflammatory reactions, fibrosis, and infections with bacterial biofilm formation, the only therapeutic alternative is surgical removal of the PMMA together with the adjacent healthy tissue, resulting in permanent sequelae.^{5,8}

Inappropriate application techniques, questionable indications, inadequate PMMA volumes for the target treatment area, and poor selection of the quality of the materials can intensify these reactions. Studies⁶ show that qualified plastic surgeons or dermatologists who understand the anatomy of the area to be treated, master the correct technique, and know how to treat potential complications should perform the procedure; however, these recommendations are often not considered.

As such, a broad investigation in the medical literature is required to compile the available scientific evidence on PMMA, determine the potential immediate and delayed complications resulting from its use, increase the understanding of PMMA safety for esthetic purposes, and question the approval of its use by the competent bodies.

Objective

In the present study, we conducted an integrative review of immediate and delayed complications resulting from PMMA reported in the literature over the last 20 years.

Materials and Methods

The present is an integrative review of the literature covering case reports and case series on immediate and delayed PMMA-related complications. We searched for articles published from 2004 to 2024 in the PubMed, Scientific Electronic Library Online (SciELO), and Scopus databases using the descriptors polymethyl methacrylate, dermal fillers, and complications.

We excluded from the review studies published outside the stipulated period, experimental studies, and studies not conducted in humans. Two independent reviewers fully read the studies meeting the inclusion criteria and, in case of conflict, a third researcher solved the discrepancy.

We extracted the following data from the articles: journal's name, author, year, country of origin, type of study (case report or case series), casuistry, age, professional performing the procedure (physician or non-physician), injected volume, anatomical site treated, post-PMMA injection signs and symptoms, immediate complications, delayed complications, complication treatment, and whether the filler treated HIV-related lipodystrophy or was used for esthetic purposes.

Results

Overall, 38 studies met the inclusion criteria for this review, totaling 587 cases (**Fig. 1**): 17 articles were case series and 21 were individual case reports (**Table 1**);⁹ 39% of the articles (15/38) reported cases occurring in Brazil; the oldest publication⁵ dates from 2008 and the most recent one,⁹ from 2024 (**Table 2**).

Anatomical Regions and Injected Volume

The most frequent filler administration site was the malar region, followed by the nasolabial fold, the gluteal region, the lips, the nasal region, the frontal region, the face, the eyelid region, the zygomatic region, the upper limbs, the chin, the jaw, the chest, the trunk, the lower limbs, the and temporal, auricular, and penile regions (**~Table 3**). Only 2

(5%) studies reported using fillers to reconstruct antiretroviral-related lipodystrophy.^{30,33} Most studies (89.4%) did not report the volume injected during the procedure; however, quantities ranged from 1.9 mL for the eyelid region in one patient,¹⁰ 4 mL for facial treatment,¹⁷ and 2 cases of gluteal filling injecting 400 mL and 900 mL of PMMA.^{3,27}

Professional Performing the Procedure

In total, 6 out of 38 studies reported the professionals performing the procedure. In 27 cases, physicians performed the procedure, including 16 certified plastic surgeons, 9 dermatologists, and 2 urologists. Six filler procedures were performed by non-physicians, including nurses, estheticians, and dentists.^{3,5,11,13,28,31}

Complications

The reported complications were divided into immediate (up to 30 days after PMMA injection) and delayed (after 30 days). Ten different immediate complications occurred; erythema was the most frequent (26%), followed by pruritus (16%), edema (11%), acute renal failure (11%), nodules (11%), and other less frequent conditions (**-Table 4**).

Thirty different delayed complications were reported. The most common delayed complication was granuloma (21%), followed by nonspecific nodules (14%), skin abnormalities (8%), inflammatory reactions (6%), edema (6%), infection (5%), necrosis (4%), facial irregularities (4%), hypercalcemia (3%), ocular involvement (3%), and chronic renal failure (3%), among others (**~Table 4**).

Treatment

treatments The three frequent included most steroids, 3,7,9-11,13,14,17,18,21,24,26-28,30,32,33,35,36,38,39,41-43 antibiotics^{3,11,20,25,29,40,42,43} and surgeries,^{3,7,9,10,12,13,17,23} ^{24,26–28,35,36,38–40,42} including 75 cases of excision. Other reported therapeutic approaches included laser,^{9,15,19,21,22} fluorouracil,^{9,14,28} ozone,⁹ xylitol,⁹ allopurinol,⁹ methotrexate,¹⁷ vitamin D,¹⁷ hydroxychloroquine,¹⁷ colchicine,²¹ hemodyalisis,^{7,29} vasopressor support,²⁹ orotracheal intubation with ventilatory support,²⁹ calcitonin,^{32,33} saline infusion,³² bisphosphonates,^{30,32,33} cyclophosphamide,³³ ketoconazole,³³ and hyaluronic acid,^{36,41} selected according to each case.

Discussion

Some literature reviews⁵ highlight the large number of complications resulting from PMMA fillers. In the present study, we updated the evidence regarding the number of complication reports resulting from PMMA use in the last 20 years. We identified a significant prevalence of cases occurring in Brazil, representing more than 50% of the total articles in the current review. Regulatory factors related to the history of Brazilian public health policy in the treatment of HIV/AIDS patients may explain these findings.

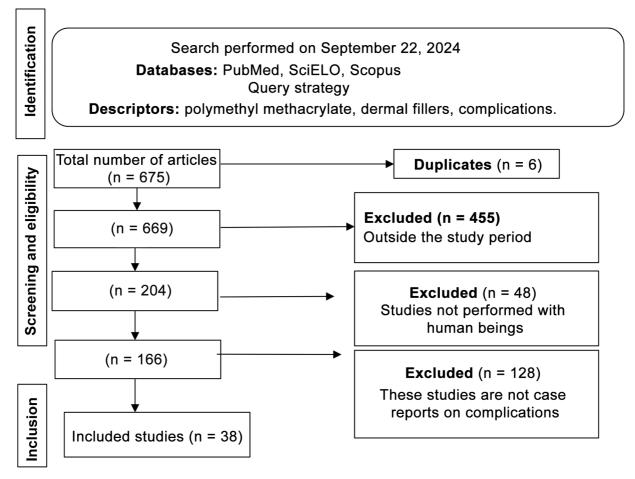


Fig. 1 Screening of the articles included in the review.

In 1996, the emergence of highly-active antiretroviral treatment improved the health condition of HIV/AIDS patients but also resulted in stigmatizing anatomical changes.⁴⁴ To address this issue, the Brazilian National Health Regulatory Agency (Agência Nacional de Vigilância Sanitária, ANVISA, in Portuguese) authorized the use of PMMA fillers for reparative purposes in this population.⁴⁵

The evolution of antiretroviral drugs decreased the number of patients with stigmatizing lipodystrophies. However, it is intriguing to note that the number of complications related to the esthetic use of PMMA has increased. In the current review, only two cases of complications resulted from PMMA use for reparative purposes in the treatment of HIV/AIDS patients.^{30,33}

Our findings show that the current use of PMMA exceeds its established safe limits and formal indications determined by regulatory agencies. For instance, we detected case reports of gluteal fillers with volumes of up to 900 mL of PMMA,³ while the Brazilian consensual recommendation published by Souza et al.⁴⁶ in 2017 is not to exceed the maximum volume of 100 mL in this region.

As such, it is important to highlight some points regarding the authorization of PMMA use for esthetic purposes. The lack of appropriate supervision results in inappropriate practices in PMMA use, such as procedures performed by non-medical professionals or untrained physicians, and in sites with inadequate infrastructure.^{3,5,11,13,28,31} Most articles, except for 6, did not identify the filler prescriber. Out of 34 cases, only 16 were performed by professionals certified for PMMA application, potentially increasing the procedural risk.⁵

From 2004 to 2024, the number of PMMA-related complications in Brazil was significantly higher compared with the rest of the world, totaling 373 cases. Although PMMA use for esthetic purposes has been questioned by the Brazilian Society of Plastic Surgery (Sociedade Brasileira de Cirurgia Plástica, SBCP, in Portuguese)⁴⁷ this material remains widely employed as a filler in Brazil. In contrast, other countries often use different reversible and absorbable fillers, such as hyaluronic acid, autologous fat grafts, poly-L-lactic acid, and collagen biostimulators.⁴⁸

The reports included more cases of delayed complications compared with immediate complications. The most frequent delayed complication was granulomatous formations (21%). It is worth noting the potential severity of the complications related to PMMA fillers, such as septic shock and chronic renal failure.^{7,21,29} In addition, the long-term safety of PMMA is uncertain, since there are reports¹² of foreign body granulomas in regions distant from the PMMA injection site. Therefore, to potentially reduce the incidence of adverse

Table 1 Articles included in the present review	Table 1	Articles	included	in the	present review
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Journal	Author	Year	Casuistry	Reference
Revista Brasileira de Cirurgia Plástica	Goldman et al.	2024	209	9
Annals of Plastic Surgery	Durkin et al.	2023	3	10
Journal of the American Academy of Dermatology	Vengalil et al.	2023	1	11
Cytopathology	Saoud et al.	2023	1	12
Ophthalmic Plastic and Reconstructive Surgery	Parikh et al.	2023	1	13
Journal of Cutaneous and Aesthetic Surgery	Sivam et al.	2023	1	14
Journal of Drugs in Dermatology	Goldman et al.	2021	27	15
SKIN The Journal of Cutaneous Medicine	Dhaliwal et al.	2021	1	16
European Review for Medical and Pharmacological Sciences	Freire de Carvalho et al.	2021	1	17
Annals of Medicine and Surgery	Alimoradi et al.	2021	1	18
Brazilian Journal of Nephrology	Manfro et al.	2021	2	7
Revista Brasileira de Cirurgia Plástica	Kurimori et al.	2019	1	3
Dermatologic Therapy	Goldman and Wollina	2019	2	19
Dermatologic Surgery	Ibrahim and Dover	2018	1	20
Georgian Medical News	Goldman et al.	2018	2	21
Open Access Macedonian Journal of Medical Sciences	Goldman and Wollina	2018	81	22
Contact Dermatitis	Shah et al.	2017	1	23
Revista Brasileira de Cirurgia Plástica	Souza et al.	2016	1	24
Diagnostic Pathology	Cannata-Ortiz et al.	2016	1	25
Aesthetic Surgery Journal	Limongi et al.	2016	11	26
Plastic Reconstructive Surgery – Global Open	Purnell et al.	2016	1	27
Journal of Cosmetic & Laser Therapy	Friedmann et al.	2016	4	28
Medicina Intensiva	Boattini et al.	2015	1	29
Calcified Tissue International	Hindi et al.	2015	1	30
Skin Research and Technology	Cinotti et al.	2015	1	31
Archives of Endocrinology and Metabolism	Rados and Furlanetto	2015	1	32
Clinical Cases in Mineral and Bone Metabolism	Negri et al.	2014	4	33
Journal of the American Geriatrics Society	Costa et al.	2014	1	34
Aesthetic Plastic Surgery	Park et al.	2012	13	35
Journal of Plastic, Reconstructive & Aesthetic Surgery	Park et al.	2012	15	36
The Canadian Journal of Plastic Surgery	Solomon et al.	2012	153	37
Journal of Hand Surgery	Al-Qattan	2011	3	38
Journal of Plastic, Reconstructive & Aesthetic Surgery	Santana et al.	2010	1	39
Aesthetic Plastic Surgery	de Figueiredo et al.	2010	1	40
Kosmetische Medizin	Wollina	2009	1	41
Plastic and Reconstructive Surgery	Salles et al.	2008	32	5
Dermatology	Wolfram et al.	2006	4	42
Clinical and Experimental Dermatology	Sidwell et al.	2006	1	43
Total				1

effects, stricter monitoring of the distribution, sale, prescription, and procedural sites is required, in addition to raising public awareness of PMMA-related risks.⁶

In Brazil, ANVISA authorizes PMMA application in two situations: correction of lipodystrophy resulting from antiretroviral medications and volumetric correction of the

Author	Year	Number of cases	Reference
Goldman et al.	2024	209	9
Goldman et al.	2021	27	15
Freire de Carvalho	2021	1	17
Manfro et al.	2021	2	7
Kurimori et al.	2019	1	3
Goldman and Wollina	2019	2	19
Goldman et al.	2018	2	21
Goldman and Wollina	2018	81	22
Souza et al.	2016	1	24
Limongi et al.	2016	11	26
Rados and Furlanetto	2015	1	32
Costa et al.	2014	1	34
Santana et al.	2010	1	39
de Figueiredo et al.	2010	1	40
Salles et al.	2008	32	5
Total		373	

Table 2 Brazilian studies included in the present review

face and body. Although there is no contraindication to PMMA use in the buttocks, it should not occur for volume increase. Only properly-qualified physicians must perform the application and decide, based on a detailed evaluation, the dosage and number of injections appropriate for each patient, considering the particularities and needs of the subject.⁴⁹

It is worth noting that ANVISA classifies PMMA as an implantable medical product of risk class IV. This classification presupposes a high level of regulatory control due to the potential risks of complications, such as inflammatory reactions, infections, material migration, and tissue necrosis, especially because PMMA is a permanent material that is not resorbable by the body, highlighting the irreversibility of this filling method.⁴⁹

Safer alternatives to PMMA include hyaluronic acid and autologous fat. Hyaluronic acid presents greater biocompatibility, a lower risk of complications, and the possibility of reversal by applying the enzyme hyaluronidase. Autologous fat is another viable and safe option with a lower complication risk.⁵⁰

The limitations of the current review include the uncertainty as to whether the higher complication incidence in Brazil results from a higher frequency of PMMA procedures or an actual higher incidence of complications. This is a significant limitation, since we do not have absolute data on the total number of procedures performed in Brazil and worldwide. Another limitation is that the review is based only on cases of complications documented in the literature, which may not reflect reality. The number of complications is likely much higher than reported, since complications not published in scientific articles could not be included.

Anatomical region	Number of studies (percentage)	Reference
Malar	12 (0.13)	5,9,11,13,14,19,20,28,35,39,42,43
Nasolabial fold	11 (0.12)	9,20,24,28,31,35,37,39-42
Gluteus	10 (0.11)	3,5,7,18,21,27,29,30,32,33
Nose	8 (0.09)	5,9,15,19,23,28,37,40
Frontal	8 (0.09)	5,9,11,12,28,35,37,42
Lip	7 (0.08)	9,13,19,28,35,37,42
Face (undetermined specific location)	7 (0.08)	16,19,22,26,35,39,43
Ocular	4 (0.04)	9,10,35,42
Zygomatic	4 (0.04)	9,17,42,43
Upper limbs	4 (0.04)	7,19,21,38
Mentum	4 (0.04)	9,13,28,42
Mandibular	2 (0.02)	9,19
Trunk	2 (0.02)	5,22
Lower limbs	2 (0.02)	25,33
Thorax	1 (0.01)	21
Temporal	1 (0.01)	9
Auricular	1 (0.01)	9
Penis	1 (0.01)	5

Table 3 Anatomical regions for polymethyl methacrylate filling

 Table 4 Immediate and delayed complications

Immediate		
Туре	Number of studies (percentage)	Reference
Erythema	5 (0.26)	13,23,37,38,42
Pruritus	3 (0.16)	23,37,40
Edema	2 (0.11)	23,38
Acute kidney failure	2 (0.11)	3,29
Nodule formation	2 (0.11)	35,42
Septic shock	1 (0.05)	29
Hepatic dysfunction	1 (0.05)	29
Ecchymosis	1 (0.05)	37
Respiratory failure	1 (0.05)	29
Seropurulent secretion	1 (0.05)	40
Delayed		
Туре	Number of studies (percentage)	Reference
Granuloma	17 (0.21)	5,9,10,12-14,16,18,21,22,26,30,33,38,39,41,42
Nodule formation	11 (0.14)	9,11,19,24,26,28,31,34,35,37,43
Skin abnormalities	6 (0.08)	25–28,38,42
Inflammatory signs	5 (0.06)	5,9,32,36,38
Edema	5 (0.06)	9,13,20,25,26
Infection	4 (0.05)	9,17,28,42
Necrosis	3 (0.04)	5,9,40
Facial irregularity	3 (0.04)	26,36,42
Hypercalcemia	2 (0.03)	18,33
Ocular involvement	2 (0.03)	13,17
Chronic kidney failure	2 (0.03)	7,21
Reduced renal function	1 (0.01)	33
Neovascularization	1 (0.01)	9
Pigmentation	1 (0.01)	9
Lacrimation	1 (0.01)	9
Fistula	1 (0.01)	9
Allergic reaction	1 (0.01)	13
Psoriasis	1 (0.01)	17
Nephrocalcinosis	1 (0.01)	18
Pulmonary granulomatous lymphadenitis	1 (0.01)	18
Pericarditis	1 (0.01)	21
Sarcoidosis-like syndrome	1 (0.01)	21
Erythema	1 (0.01)	26
Tachycardia	1 (0.01)	27
Hyperkalemia	1 (0.01)	32
Nephritis	1 (0.01)	33
Pruritus	1 (0.01)	33
Hypertension	1 (0.01)	33
Rigidity	1 (0.01)	36
Seroma	1 (0.01)	38
Pulmonary sarcoidosis	1 (0.01)	43

Conclusion

Polymethyl methacrylate fillers are associated with serious immediate and delayed complications. Most complications are not related to their use for the correction of lipodystrophies in patients with HIV/AIDS. Most (64%) complications described in the medical literature over the last 20 years occurred in Brazil. Polymethyl methacrylate is non-absorbable, and multiple invasive surgical procedures may be required to treat the sequelae resulting from its use as a permanent filler. There are alternatives to PMMA that are reversible and present lower risks to the health of patients.

Authors' contributions

MMCS: data analysis and/or interpretation, final manuscript approval, conceptualization, study conception and design, methodology, writing – original draft preparation, writing – review & editing, and supervision; ALC: data analysis and/or interpretation, statistical analysis, study conception and design, methodology, writing – original draft preparation, and writing – review & editing; LHMCV: methodology, writing – original draft preparation, and writing – review & editing; PBSM: data analysis and/or interpretation, writing – original draft preparation, and writing – review & editing; IMAS: statistical analysis, writing – original draft preparation, and writing – review & editing; and MARM: final manuscript approval, project management, writing – review & editing, and supervision.

Clinical Trials

None.

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Conflict of Interests

The authors have no conflict of interests to declare.

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