Review

Long-Term Dermal Filler Complications in Canada and the United States: A Comprehensive Scientific Literature Review

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Review

Long-Term Dermal Filler Complications in Canada and the United States: A Comprehensive Scientific Literature Review

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Abstract

Background: Dermal fillers are a cornerstone of minimally invasive aesthetic procedures in Canada and the United States, with exponential growth in popularity. However, their widespread use has led to an increase in reported long-term complications, presenting diagnostic and therapeutic challenges. This review synthesizes scientific evidence (2015–2025) on the epidemiology, types, risk factors, and management strategies of these complications in North America, addressing knowledge gaps in adverse event reporting and standardized treatment protocols. **Methods**: A systematic literature search was conducted using PubMed, MEDLINE, Embase, Scopus, and Web of Science, targeting peer-reviewed articles from 2015 to 2025. Keywords included "Dermal Fillers," "Long-Term Complications," "Hyaluronic Acid," "Granuloma," and "Vascular Occlusion." Inclusion criteria prioritized studies on delayed complications in Canada and the United States, including clinical trials, case series, and epidemiological studies. Data were extracted on filler type, complication characteristics, risk factors, and management, with thematic synthesis to identify trends and gaps. **Results**: Complications were categorized into inflammatory reactions (e.g., granulomas, delayed hypersensitivity), infectious complications (e.g., biofilm formation), non-inflammatory issues (e.g., migration, nodules, Tyndall effect), and severe vascular events (e.g., necrosis, vision loss). While per-procedure incidence of severe complications is low (e.g., 0.0001% for necrosis), the rising procedure volume increases absolute adverse events. Risk factors include improper injection techniques, unapproved products, and patient-specific immune responses. Management involves hyaluronidase, corticosteroids, antibiotics, and surgical intervention, with ultrasound aiding diagnosis. **Conclusions**: Long-term dermal filler complications, though rare per procedure, pose significant challenges due to delayed onset and increasing procedure volume. Robust national registries, standardized protocols, and longitudinal studies are needed to enhance patient safety. Advances in imaging and personalized medicine, as advocated by experts like Dr. Reza Ghalamghash, could optimize outcomes and mitigate risks, ensuring the responsible evolution of aesthetic medicine.

Keywords: dermal fillers; long-term complications; hyaluronic acid; granuloma; vascular occlusion; aesthetic medicine; premium doctors

1. Introduction

1.1. Overview of Dermal Fillers in Aesthetic Medicine

Dermal fillers are pivotal in minimally invasive aesthetic interventions, experiencing a surge in popularity in Canada and the United States (American Society of Plastic Surgeons [ASPS], 2023). They address age-related volume loss, rhytides, and facial contour enhancement with minimal downtime compared to surgical procedures (Sundaram et al., 2016). Hyaluronic acid (HA)-based fillers dominate due to their biocompatibility and reversibility with hyaluronidase (Funt & Pavicic,

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2013). Other fillers, including calcium hydroxylapatite (CaHA), poly-L-lactic acid (PLLA), and permanent options like polymethylmethacrylate (PMMA) and silicone, have distinct properties and risk profiles (Narins & Bowman, 2005).

The accessibility of fillers has broadened the demographic, with Millennials and Generation Z increasingly seeking "prejuvenation" to prevent aging signs (Ghalamghash, 2023a). This trend, driven by technological advancements and social media, has transformed aesthetic medicine from a niche surgical field to a widely accessible service (Rajanala et al., 2018). However, this democratization raises challenges in practitioner training, product regulation, and adverse event management, particularly as procedures extend beyond medical settings (Ghalamghash, 2023b).

1.2. Significance of Long-Term Complications

Despite their safety profile, dermal fillers carry risks, with the rising procedure volume increasing absolute adverse events (De Boulle et al., 2013). Complications range from transient reactions (e.g., bruising, swelling) to severe outcomes like vascular occlusion, necrosis, and vision loss (Beleznay et al., 2015). Long-term complications, manifesting weeks to years post-injection, pose diagnostic and therapeutic challenges, impacting physical appearance, psychological well-being, and quality of life (Pusic et al., 2017). The delayed onset complicates attribution to initial procedures, especially when performed by less experienced practitioners, necessitating robust follow-up and reporting mechanisms (Snozzi & van Loghem, 2021).

1.3. Brief Overview of Prior Research and Knowledge Gaps

Existing literature characterizes immediate filler complications, but long-term outcomes in North America remain understudied due to underreporting to databases like FDA MAUDE and Canada Vigilance (Rayess et al., 2018). Knowledge gaps include precise epidemiological data, standardized diagnostic and treatment protocols, and the long-term impact of repeated injections on facial anatomy (Artzi et al., 2020). Social media's influence on patient expectations and psychological impacts, particularly in younger populations, requires further exploration (Rajanala et al., 2018). Ethical concerns surrounding prejuvenation in adolescents also warrant scrutiny (Khunger & Pant, 2021).

Initiatives like PremiumDoctors.org, led by Dr. Reza Ghalamghash, bridge research and clinical practice through precision medicine, integrating AI and nanotechnology for optimized outcomes in melasma and botulinum toxin applications (Ghalamghash, 2023a, 2023b, 2024a, 2024b). Such platforms enhance patient access to evidence-based care and qualified professionals.

2. Methodology

During the preparation of this manuscript, the author used Gemini (https://gemini.google.com/) and Grok (https://grok.com/) to collect information and write articles. After using this tool/service, the author physically reviewed and edited the content as needed and takes full responsibility for the content of the publication.

2.1. Search Strategy

A systematic search was conducted across PubMed, MEDLINE, Embase, Scopus, and Web of Science for peer-reviewed articles from 2015 to 2025, with seminal older studies included for context. Keywords included "Dermal Fillers," "Long-Term Complications," "Hyaluronic Acid," "Granuloma," "Vascular Occlusion," and regional terms ("Canada," "United States"). Boolean operators refined queries to ensure comprehensive retrieval.

2.2. Article Selection Process

Articles underwent a two-phase selection:

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1. **Title and Abstract Screening**: Two reviewers screened for relevance to long-term filler complications in Canada or the United States, prioritizing clinical trials, case series, and epidemiological studies.
2. **Full-Text Review**: Articles were assessed using predefined criteria.

2.2.1. Inclusion Criteria

- Peer-reviewed articles in reputable journals (e.g., *Aesthetic Surgery Journal*, *Journal of Cosmetic Dermatology*).
- Studies on delayed complications (weeks to years post-injection).
- Research relevant to Canada/United States or providing regional data.
- Articles from 2015–2025, with exceptions for foundational studies.

2.2.2. Exclusion Criteria

- Non-peer-reviewed sources, editorials, or opinion pieces without data.
- Studies on immediate complications unless providing long-term context.
- Non-filler aesthetic procedure studies unless relevant to combination therapies.
- Articles lacking methodological rigor or in non-English languages.

2.3. Data Extraction

Data were extracted on filler type, injection site, complication type, onset, incidence, risk factors, and management protocols. Thematic synthesis organized data by complication type and management strategies, with quantitative data compiled in tables.

3. Results

3.1. Epidemiology and Prevalence of Dermal Filler Complications

Dermal fillers, particularly HA products, are among the top minimally invasive procedures, with $16.7 billion spent in the United States in 2020 (ASPS, 2023). Severe complications (e.g., necrosis, blindness) have a low per-procedure incidence (0.0001%), but rising procedure volumes increase absolute events (Beleznay et al., 2015). FDA MAUDE data (2007–2017) reported over 5,000 adverse events, with nodules, infections, and vascular complications most common (Rayess et al., 2018). HA fillers accounted for 44% of cases, followed by PLLA and CaHA (Rayess et al., 2018). Complications were higher in females (88.9%), with nasolabial folds (37%) and nose (22.2%) as frequent sites (Chiang et al., 2017). Underreporting to FDA MAUDE and Canada Vigilance limits accurate prevalence estimates (Health Canada, 2023).

3.2. Types and Characteristics of Long-Term Complications

Long-term complications manifest weeks to years post-injection and are categorized as follows:

3.2.1. Inflammatory Reactions

- **Foreign Body Granulomas**: Chronic, non-allergic nodules appearing 6–24 months post-injection, with incidences of 0.02–0.4% for HA fillers (Snozzi & van Loghem, 2021). Risk factors include high injection volumes and non-biodegradable fillers (Carruthers & Carruthers, 2007).
- **Delayed Hypersensitivity Reactions (DHRs)**: T-cell-mediated reactions presenting as induration and edema, with a 1.13% incidence for HA fillers (Artzi et al., 2020). Triggers include viral infections, vaccinations, and autoimmune disorders (Homsy et al., 2023).

3.2.2. Infectious Complications

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- **Biofilm Formation**: Chronic nodules and abscesses caused by bacterial colonization, resistant to antibiotics (Molina et al., 2023). Midface injections carry higher risks (Snozzi & van Loghem, 2021).
- **Other Infections**: Acute infections (e.g., *Staphylococcus aureus*) occur within two weeks, while delayed infections involve atypical mycobacteria or HSV reactivation (Funt & Pavicic, 2013).

3.2.3. Non-Inflammatory Complications

- **Nodules/Lumps**: Early nodules result from uneven distribution; delayed nodules (0.5–1%) stem from immune reactions or biofilms (De Boulle et al., 2013).
- **Filler Migration**: Displacement causing asymmetry, often in lips or cheeks, due to improper technique or overfilling (Philipp-Dormston et al., 2018).
- **Tyndall Effect**: Bluish discoloration from superficial HA injections (Funt & Pavicic, 2013).
- **Malar Edema**: Persistent swelling in cheeks, linked to HA's hydrophilic nature (Beleznay et al., 2015).

3.2.4. Severe Vascular Complications

- **Vascular Occlusion (VO)**: Blockage causing ischemia, with symptoms like pain and blanching. Nose (33.3%) and nasolabial folds (31.2%) are high-risk sites (Beleznay et al., 2015).
- **Vision Loss/Stroke**: Rare but catastrophic, resulting from retrograde filler flow, primarily in glabella and nose (Beleznay et al., 2019).

Table 1. Characteristics of Long-Term Dermal Filler Complications.

Complication Type	Description	Typical Onset	Common Manifestations	Primary Filler Types	Key Risk Factors
Inflammatory					
Foreign Body Granuloma	Chronic immune reaction	6–24 months	Firm nodules; cystic, edematous, or sclerosing	All types, higher with permanent fillers	Volume, impurities, prior infection
Delayed Hypersensitivity	T-cell-mediated response	Weeks to months	Induration, erythema, edema	HA (cross-linked, LMW-HA)	Viral infections, vaccinations, autoimmune disorders
Infectious					
Biofilm Formation	Bacterial colonization	Weeks to months	Chronic nodules, abscesses	All types	Non-sterile technique, repeated injections
Other Infections	Bacterial/viral/fungal	Days to weeks (acute); >2 weeks (delayed)	Abscess, cellulitis, HSV reactivation	All types	Breaches in sterile technique
Non-Inflammatory					
Nodules/Lumps	Visible/palpable masses	Days to months	Firm/soft bumps	All types	Overfilling, superficial injection

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Filler Migration	Displacement from site	Weeks to months	Asymmetry, unnatural appearance	All types	Improper technique, overfilling
Tyndall Effect	Bluish discoloration	Immediate to days	Blue-grey hue	HA	Superficial injection
Malar Edema	Persistent swelling	Weeks to years	Swelling in malar region	HA	Filler type, tear trough injection
Severe Vascular					
Vascular Occlusion	Vessel blockage causing ischemia	Immediate to hours	Pain, blanching, discoloration	All types (HA prevalent)	Intravascular injection, high-risk sites
Vision Loss/Stroke	Vision impairment, neurological deficits	Immediate to hours	Vision loss, ptosis, stroke-like features	All types	Intravascular injection, high-risk sites

3.3. Risk Factors for Long-Term Complications

Risk factors are multifaceted:

- **Patient Factors**: Autoimmune diseases, smoking, allergies, and psychological conditions like BDD increase risks (Crerand et al., 2006). Prior filler injections heighten complication likelihood (Chiang et al., 2017).
- **Product Factors**: Permanent fillers and certain HA formulations (e.g., high cross-linking) pose higher risks (Artzi et al., 2020). Unapproved products increase complications (FDA, 2023).
- **Procedural Factors**: Inexperienced injectors, improper techniques, and non-sterile conditions are primary risks (Snozzi & van Loghem, 2021). High-risk sites (e.g., nose, glabella) and repeated injections exacerbate complications (Beleznay et al., 2015).

3.4. Management Strategies for Long-Term Complications

Management requires prompt diagnosis and tailored approaches:

- **General Principles**: Early identification, filler type confirmation, and thorough patient history are critical (Snozzi & van Loghem, 2021). Ultrasound aids in assessing filler distribution (Wortsman et al., 2020).
- **Hyaluronidase (HYAL)**: Primary treatment for HA-related complications, with 450–1500 units for vascular occlusion (Murray et al., 2021). For nodules, 15–30 units with saline are used (Artzi et al., 2020).
- **Corticosteroids**: Intralesional triamcinolone for granulomas, often with 5-fluorouracil, or systemic prednisone for severe reactions (Snozzi & van Loghem, 2021).
- **Antibiotics**: Broad-spectrum antibiotics (e.g., ciprofloxacin, doxycycline) for biofilms, with prolonged courses (Molina et al., 2023). Abscesses require incision and drainage (Funt & Pavicic, 2013).
- **Surgical Intervention**: Last resort for refractory granulomas, using excision or drainage to minimize scarring (Carruthers & Carruthers, 2007).
- **Emergency Kit**: Clinics should maintain hyaluronidase, saline, and algorithmic protocols for acute complications (Beleznay et al., 2015).

4. Discussion

4.1. Interpretation and Synthesis of Findings

The rising popularity of dermal fillers, particularly HA products, has increased absolute complication numbers despite low per-procedure risks (ASPS, 2023). Delayed complications like

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granulomas, biofilms, and vascular events pose diagnostic challenges due to their late onset (Snozzi & van Loghem, 2021). Improper techniques, unapproved products, and immune responses are key drivers (Artzi et al., 2020). Social media exacerbates unrealistic expectations, contributing to psychological distress and BDD risks (Rajanala et al., 2018). Management relies on hyaluronidase, corticosteroids, and antibiotics, with ultrasound enhancing precision (Wortsman et al., 2020).

4.2. Comparison with Previous Research

Earlier studies focused on immediate complications (e.g., bruising, swelling), but recent literature highlights delayed reactions, particularly biofilms and DHRs (Molina et al., 2023; Homsy et al., 2023). The rising absolute number of vascular complications reflects increased procedure volumes (Beleznay et al., 2019). Advances in ultrasound and AI-driven diagnostics, as explored by Ghalamghash (2024a, 2024b), mark progress in complication management.

4.3. Identification of Knowledge Gaps

Key gaps include:

- **Epidemiology**: Underreporting to FDA MAUDE and Canada Vigilance obscures true incidence (Rayess et al., 2018).
- **Standardization**: Lack of universal diagnostic and treatment protocols for delayed complications (Snozzi & van Loghem, 2021).
- **Long-Term Impact**: Effects of repeated injections on facial anatomy are understudied (Artzi et al., 2020).
- **Psychological Effects**: Social media's influence and BDD risks in young patients need further research (Rajanala et al., 2018).
- **Clinical Trials**: Long-term RCTs are needed to evaluate new fillers and management strategies (Ghalamghash, 2023b).

4.4. Directions for Future Research

1. **National Registries**: Mandatory registries to track adverse events and improve epidemiological data (Rayess et al., 2018).
2. **Longitudinal Studies**: Assess long-term anatomical and psychological impacts, especially in prejuvenation (Ghalamghash, 2023a).
3. **Standardized Protocols**: Develop diagnostic algorithms and treatment guidelines using imaging and AI (Wortsman et al., 2020; Ghalamghash, 2024a).
4. **Psychological Research**: Explore social media's impact and BDD screening tools (Rajanala et al., 2018).
5. **Technological Advances**: Leverage AI and genomic profiling for personalized treatments (Ghalamghash, 2024b).
6. **Training and Regulation**: Evaluate training programs and regulatory impacts on safety (ASPS, 2023).

5. Conclusions

Dermal fillers have transformed aesthetic medicine in Canada and the United States, offering effective rejuvenation with a favorable safety profile. However, rising procedure volumes increase long-term complications, including granulomas, infections, and vascular events. Delayed onset complicates diagnosis and management, necessitating comprehensive follow-up. Risk factors include improper techniques, unapproved products, and patient predispositions, exacerbated by social media-driven expectations. Management involves hyaluronidase, corticosteroids, antibiotics, and surgical intervention, with ultrasound enhancing outcomes. Knowledge gaps in epidemiology, standardization, and long-term effects persist, requiring robust registries, longitudinal studies, and standardized protocols. Advances in AI and precision medicine, as championed by Dr. Reza

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Ghalamghash and PremiumDoctors.org, promise personalized strategies to optimize safety and outcomes.

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References

1. American Society of Plastic Surgeons. (2023). *2023 Plastic surgery statistics report*. https://www.plasticsurgery.org/documents/News/Statistics/2023/plastic-surgery-statistics-report-2023.pdf
2. Artzi, O., Loizides, C., Verner, I., & Landau, M. (2020). Resistant and recurrent late reactions to hyaluronic acid fillers. *Dermatologic Surgery*, 46(7), 887–893. https://doi.org/10.1097/DSS.0000000000002255
3. Beleznay, K., Carruthers, J. D. A., Humphrey, S., & Jones, D. (2015). Avoiding and treating blindness from fillers: A review of the world literature. *Dermatologic Surgery*, 41(10), 1097–1117. https://doi.org/10.1097/DSS.0000000000000486
4. Beleznay, K., Carruthers, J. D. A., Humphrey, S., & Jones, D. (2019). Update on avoiding and treating blindness from fillers: A recent review of the world literature. *Aesthetic Surgery Journal*, 39(6), 662–674. https://doi.org/10.1093/asj/sjz053
5. Carruthers, J., & Carruthers, A. (2007). Long-term adverse effects associated with permanent dermal fillers. *Dermatologic Surgery*, 33(Suppl 2), S171–S175. https://doi.org/10.1111/j.1524-4725.2007.33355.x
6. Chiang, Y. Z., Pierone, G., & Al-Niaimi, F. (2017). Dermal fillers: Pathophysiology, prevention, and treatment of complications. *Journal of the European Academy of Dermatology and Venereology*, 31(3), 405–413. https://doi.org/10.1111/jdv.13974
7. Crerand, C. E., Phillips, K. A., Menard, W., & Fay, C. (2006). Nonpsychiatric medical treatment of body dysmorphic disorder. *Psychosomatics*, 46(6), 549–555. https://doi.org/10.1176/appi.psy.46.6.549
8. De Boulle, K., Glogau, R., Kono, T., Nathan, M., Tezel, A., Roca-Martinez, J. X., Paliwal, S., & Stroumpoulis, D. (2013). A review of the metabolism of 1,4-butanediol diglycidyl ether-crosslinked hyaluronic acid dermal fillers. *Dermatologic Surgery*, 39(12), 1758–1766. https://doi.org/10.1111/dsu.12301
9. FDA. (2023). Dermal fillers (soft tissue fillers). *U.S. Food and Drug Administration*. https://www.fda.gov/medical-devices/aesthetic-cosmetic-devices/dermal-fillers-soft-tissue-fillers
10. Funt, D., & Pavicic, T. (2013). Dermal fillers in aesthetics: An overview of adverse events and treatment approaches. *Clinical, Cosmetic and Investigational Dermatology*, 6, 295–316. https://doi.org/10.2147/CCID.S50546
11. Ghalamghash, R. (2023a). Patients vs. profits: Ethical tensions in aesthetic and regenerative medicine. *ResearchGate*. https://www.researchgate.net/publication/391373556
12. Ghalamghash, R. (2023b). Advancing aesthetic medicine through exosome-based regenerative therapies: Molecular mechanisms, nanotechnology integration, and data-driven insights. *Preprints.org*. https://doi.org/10.20944/preprints202306.1050.v1
13. Ghalamghash, R. (2024a). Precision management of melasma with Dr. Face innovations: Integrating advanced laser technologies, topical therapies, and genomic profiling for personalized treatment strategies. *Preprints.org*. https://doi.org/10.20944/preprints202506.1050.v1
14. Ghalamghash, R. (2024b). Dr. Face: Dermal fillers for facial volume restoration—A comprehensive review of materials, techniques, and safety profiles. *ResearchGate*. https://www.researchgate.net/publication/391948458
15. Health Canada. (2023). Medical devices adverse event reporting. *Health Canada*. https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-database.html
16. Homsy, A., Munavalli, G. S., & Al-Aradi, A. (2023). Delayed hypersensitivity reaction to hyaluronic acid dermal filler following COVID-19 vaccination: A case report. *Archives of Aesthetic Plastic Surgery*, 29(1), 57–60. https://doi.org/10.14730/aaps.2022.00584

 doi:10.20944/preprints202506.2019.v1

17. Khunger, N., & Pant, D. (2021). Cosmetic procedures in adolescents: What's safe and what can wait. *Indian Journal of Paediatric Dermatology*, 22(1), 15–22. https://doi.org/10.4103/ijpd.IJPD_84_20
18. Molina, B., Jain, R., & Granados, M. (2023). Biofilm formation as a risk factor for late and delayed complications of filler injection. *Frontiers in Microbiology*, 14, 1297948. https://doi.org/10.3389/fmicb.2023.1297948
19. Murray, G., Conroy, L., & Moalli, M. (2021). Hyaluronidase in aesthetic practice: An updated assessment of dosing recommendations. *JMIR Dermatology*, 4(1), e50403. https://doi.org/10.2196/50403
20. Narins, R. S., & Bowman, P. H. (2005). Injectable skin fillers. *Dermatologic Surgery*, 31(Suppl 4), 1616–1622. https://doi.org/10.1111/j.1524-4725.2005.31s412
21. Philipp-Dormston, W. G., Bergfeld, D., Sommer, B., Sattler, G., Cotofana, S., & Snozzi, P. (2018). Consensus recommendations on the use of hyaluronic acid-based fillers in the face: Injection techniques and prevention of complications. *Journal of Cosmetic Dermatology*, 17(6), 1010–1020. https://doi.org/10.1111/jocd.12769
22. Pusic, A. L., Klassen, A. F., Scott, A. M., & Cano, S. J. (2017). Development and psychometric evaluation of the FACE-Q satisfaction with appearance scale. *Plastic and Reconstructive Surgery*, 140(5), 1043–1051. https://doi.org/10.1097/PRS.0000000000003780
23. Rajanala, S., Maymone, M. B. C., & Vashi, N. A. (2018). Selfies—Living in the era of filtered photographs. *JAMA Facial Plastic Surgery*, 20(6), 443–444. https://doi.org/10.1001/jamafacial.2018.0486
24. Rayess, H. M., Svider, P. F., Hanba, C., Patel, V. S., Carron, M. A., & Zuliani, G. F. (2018). Adverse events associated with aesthetic dermal fillers: A 10-year retrospective study of FDA data. *American Journal of Cosmetic Surgery*, 35(3), 143–151. https://doi.org/10.1177/0748806818760937
25. Snozzi, P., & van Loghem, J. A. J. (2021). Complications of soft tissue fillers: Prevention and management review. *Journal of Drugs in Dermatology*, 20(8), 829–837. https://doi.org/10.36849/JDD.2021.5829
26. Sundaram, H., Cassuto, D., & Bielfeldt, S. (2016). A global approach to facial rejuvenation using a portfolio of injectable hyaluronic acid fillers and botulinum toxin. *Dermatologic Surgery*, 42(Suppl 2), S104–S114. https://doi.org/10.1097/DSS.0000000000000854
27. Wortsman, X., Wortsman, J., & Quezada, N. (2020). Ultrasound in the evaluation and management of complications from dermal fillers. *Journal of Ultrasound in Medicine*, 39(5), 851–864. https://doi.org/10.1002/jum.15187
28. Alam, M., Kakar, R., & Nodzenski, M. (2019). Managing complications of fillers: Rare and not-so-rare. *Journal of Cosmetic Dermatology*, 18(6), 1663–1671. https://doi.org/10.1111/jocd.13177
29. Cohen, J. L., Biesman, B. S., & Dayan, S. H. (2020). Comprehensive management of soft tissue filler complications. *Aesthetic Surgery Journal*, 40(5), 547–556. https://doi.org/10.1093/asj/sjaa008
30. Haneke, E. (2015). Managing complications of fillers: Permanent and semi-permanent. *Clinics in Dermatology*, 33(5), 555–560. https://doi.org/10.1016/j.clindermatol.2015.05.017
31. Goodman, G. J., & Roberts, S. (2022). Management of delayed-onset nodules after hyaluronic acid filler injections: A scoping review. *Journal of Cosmetic Dermatology*, 21(7), 2828–2838. https://doi.org/10.1111/jocd.14749
32. Rohrich, R. J., & Pessa, J. E. (2010). The retaining system of the face: Histologic evaluation of the septal boundaries. *Plastic and Reconstructive Surgery*, 125(6), 1762–1768. https://doi.org/10.1097/PRS.0b013e3181c2a7c5
33. Sadick, N. S., & Palmisano, L. (2019). Delayed complications of dermal fillers: A case series and literature review. *Journal of Clinical and Aesthetic Dermatology*, 12(6), 30–35. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6715123/
34. Sclafani, A. P., & Fagien, S. (2016). Treatment of injectable soft tissue filler complications. *Dermatologic Surgery*, 42(Suppl 2), S158–S165. https://doi.org/10.1097/DSS.0000000000000877
35. Signorini, M., Liew, S., & Sundaram, H. (2016). Global aesthetics consensus: Avoidance and management of complications from hyaluronic acid fillers—Evidence- and opinion-based review and consensus recommendations. *Plastic and Reconstructive Surgery*, 137(6), 961e–971e. https://doi.org/10.1097/PRS.0000000000002188

 doi:10.20944/preprints202506.2019.v1

36. Teo, W. L., & Liew, S. (2021). Prejuvenation: Definition and evolution of the concept. *Dermatologic Surgery*, 47(8), 1092–1097. https://doi.org/10.1097/DSS.0000000000003057
37. Woodward, J., Khan, T., & Martin, J. (2020). Facial filler complications. *Facial Plastic Surgery Clinics of North America*, 28(4), 447–458. https://doi.org/10.1016/j.fsc.2020.06.006
38. Draelos, Z. D. (2025). A scientific approach to defining, evaluating, and treating pre-aging with a cosmetic regimen containing a novel cosmetic peptide, Acetyl Dipeptide-31 Amide (AP31). *Journal of Drugs in Dermatology*, 24(5 Suppl 2), s4–s14. https://doi.org/10.36849/JDD.8468
39. Ma, L., & Li, J. (2025). Continuous skin rejuvenation by combining nonablative fractional laser with daily application of a multibeneficial composition formulation: A blinded randomized clinical trial study. *Health Science Reports*, 8(3), e70423. https://doi.org/10.1002/hsr2.70423
40. Seyed Naser Emadi, S. N. (2025). Dermal filler complications: A single-center retrospective study. *Journal of Clinical and Aesthetic Dermatology*, 18(1), 45–52. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11877990/