European Journal of Plastic Surgery (2024) 47:49
https://doi.org/10.1007/s00238-024-02197-y

REVIEW

What do we know about Aquafilling tissue filler? – A systematic review

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Received: 1 March 2024 / Accepted: 17 April 2024

Abstract

Background The increasing popularity of minimally invasive aesthetic surgery has led to the ongoing development of new tissue fillers. These substances require a long-term safety assessment. One of the new fillers introduced to the market is a copolyamide-based gel called Aquafilling, subsequently renamed as Los Deline. In this review, we analyze the updated published information concerning this substance.

Methods 734 articles published within the last 20 years were retrieved from the databases of PubMed, Scopus, Embase, and Google Scholar. Thirty articles describing 251 patients met the inclusion criteria.

Results The most common complications were induration, firmness, pain, and gel migration. Twenty articles reported inflammation resulting from gel injection. The most common imaging method was MRI combined with USG. Six out of eight studies describing laboratory findings reported no elevation of CRP, WBC or ESR. The treatments with the lowest rates of reoperation were mastectomy and radical surgery (massive irrigation and infiltrating tissue excision). There was significant heterogeneity of pathogens obtained from gel-derived swabs.

Conclusions Over time, Aquafilling injection can potentially result in a variety of complications. It triggers inflammation and prophylactic removal should be considered. MRI and USG are recommended in the diagnostic process. Elevated CRP, WBC, or ESR indicate the presence of comorbidity or advanced gel infection. The recommended treatment is radical surgery. There is not enough information available in the literature about reconstruction, especially regarding immediate reconstruction. Antibiotics should be administered according to the antibiogram, with ciprofloxacin and clindamycin being considered if empirical treatment is needed; however, further research is required.

Level of evidence: Not ratable

Keywords Aquafilling · Tissue filler · Breast augmentation · Complications

Introduction

Body contouring is a dynamically evolving discipline with numerous achievements. The success of substances such as hyaluronic acid in subcutaneous/intradermal injections has demonstrated the potential for further research in this field; thus stimulating the search for less invasive alternatives to surgical intervention [1]. This has led to numerous attempts to use artificial liquids such as paraffin or polyacrylamide gel for breast and buttock augmentation. In theory, the injection of such substances could improve the shape of the breasts or buttocks without leaving the visible scars and strains related to surgery; therefore, it would supersede the traditional silicone implant-based augmentation. However, subsequent studies have shown that these substances lead to massive and life-threatening complications due to gel migration and its toxicity to the surrounding tissues [2, 3].

Nonetheless, each substance has to be studied separately, and the failure of one tissue filler does not imply that every product will provide the same results. Therefore, a new gel was introduced to the market under the tradename Aquafilling Bodyline (Biomedica, Spol. s.r.o., Czech Republic). According to the manufacturer, it consists of 98% solution of sodium chloride and 2% copolyamide and is supposed to be degradable [4]. Interestingly, some studies have reported that they found polyacrylamide particles in Aquafilling samples

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Published online: 03 May 2024

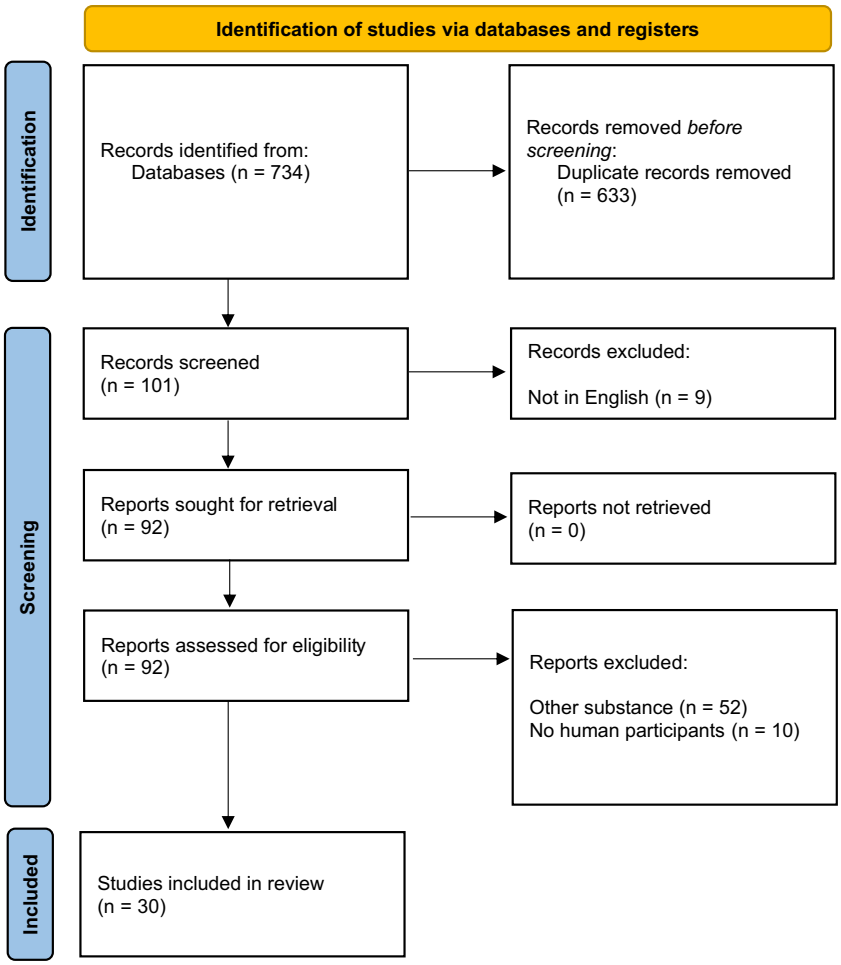

Fig. 1 PRISMA chart of the article selection process

[5]. After its introduction into the clinic, a considerable number of reports have been published describing complications following breast and buttock augmentation with the substance [6]. The product was subsequently renamed as Los Deline.

The aim of this study was to display all the information published in the latest scientific literature regarding Aquafilling/Los Deline tissue filler. The study focused mainly on data that are important from a clinical point of view; however, an attempt was also made to assess the scale of Aquafilling's distribution.

Materials and methods

The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Selected literature published within the last 20 years (n = 734) was retrieved from PubMed (National Library of Medicine), Scopus (Elsevier), Embase (Elsevier), and Google Scholar (Google, Mountain View, CA) databases. The search terms were as follows: "Aquafilling"; "Aquafilling gel"; "Aquafilling tissue filler"; "Los Deline"; "Los Deline gel"; "Los Deline tissue filler"; "Copolyamide"; "Copolyamide gel"; and "Copolyamide tissue filler".

Articles published in languages other than English were excluded. Research papers describing substances other than Aquafilling or Los Deline were rejected. Only articles with human participants were included. Invited discussions, position statements, and reviews were excluded from the statistical analysis; however, relevant information retrieved from these sources was also discussed.

GraphPad Prism 10 (GraphPad Software, La Jolla, CA, USA) was used for data processing. Statistical significance was determined using Fisher's exact test (if available). Values of $p < 0.05$ were considered significant. The inflammation chart was plotted using https://www.biorender.com.

Results and discussion

The study identification process is shown in Fig. 1. Statistical analysis was calculated based on data from 251 patients obtained from 30 articles that met the appropriate search

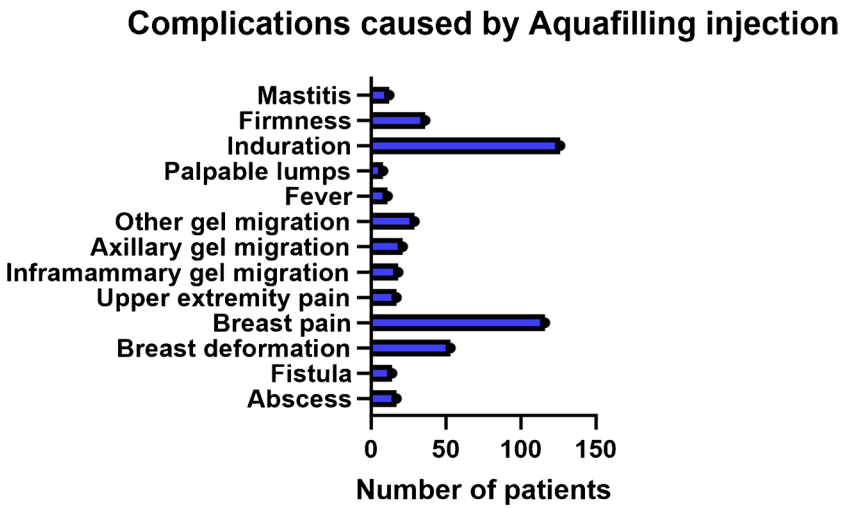

Fig. 2 Complications following the Aquafilling injection as described in the literature. Since Aquafilling is commonly used for breast augmentation, complications with the highest prevalence are breast-related

criteria. The majority of the studies included were case reports; therefore, a meta-analysis was not possible, and a descriptive review was performed.

Safety and sites of injection

There is only one article suggesting that Aquafilling is a promising tissue filler [7]. Nevertheless, the authors of the aforementioned study highlight that further research is required to assess the long-term safety of the gel. Furthermore, they believe that this may be a temporary measure, since the company claims that Aquafilling can be dissolved within the body.

The remaining literature shows that the long-term safety of the gel is questionable and its disappearance within the tissues is uncertain. Of the 30 articles that met the inclusion criteria, 29 described complications following Aquafilling injections.

Of the 251 patients described in the literature, 236 (94%) underwent breast augmentation with Aquafilling gel, 9 (3.6%) received an injection in the gluteal region, and 6 (2.4%) received a facial injection. The mean time from injection to onset of reported complications was 31.4 ± 23.9 (mean $\pm$ SD) months. The relatively long onset period of side effects from injections may partially explain the widespread use of this tissue filler since its introduction to the market.

Complications

Patients described in the literature usually suffered from more than one complication at the same time. Overall, the most common symptom was tissue induration and firmness (162 cases). The most common complications in patients after Aquafilling breast augmentation were: breast pain (116 cases), breast deformation (53 cases), axillary, and inframammary gel migration (21 and 18 cases, respectively). There were also cases of abdominal, chest wall and distal hand migrations [8]. Other common complications included formation of an abscess (17 cases), fistula (14 cases), mastitis (12 cases), and fever (11 cases). Figure 2 summarizes the complications reported in the literature.

Inflammation and prophylactic gel removal

Twenty articles (66.6%) mentioned that the gel triggered inflammation. Moreover, Chalcarz et al. reported that Aquafilling induced an inflammatory response independent of visible symptoms [9]. In the tissue exposed to Aquafilling, the expression of lymphocytes T (CD3), lymphocytes B (CD20), and macrophages (CD68) was observed. Furthermore, the gel leads to an increase in angiogenesis as well as thickening of the walls of existing vessels. Figure 3 depicts the probable mechanisms by which CD3, CD20, and CD68 cells participate in the inflammatory process within the tissues surrounding the Aquafilling containers.

Chronic inflammation causes damage to neighbouring epithelial cells, which results in increased TGFβ and Il-13 secretion. These cytokines affect surrounding myofibroblasts and fibroblasts, leading to increased Extracellular Matrix (ECM) synthesis as well as decreased Metalloproteinases expression (which also prevents ECM destruction) [10]. These changes are responsible for fibrosis and increase the risk of developing cancer. This leads to the conclusion that Aquafilling should be removed even if no symptoms are observed to prevent inflammation. However, the likelihood of neoplastic progression resulting from the presence of Aquafilling requires further examination [11].

Eight articles reported no carcinogenesis on histopathological examination following tissue excision during the Aquafilling removal procedure. In one study, invasive ductal carcinoma was found in the excised material, and another article described an atypical ductal hyperplasia

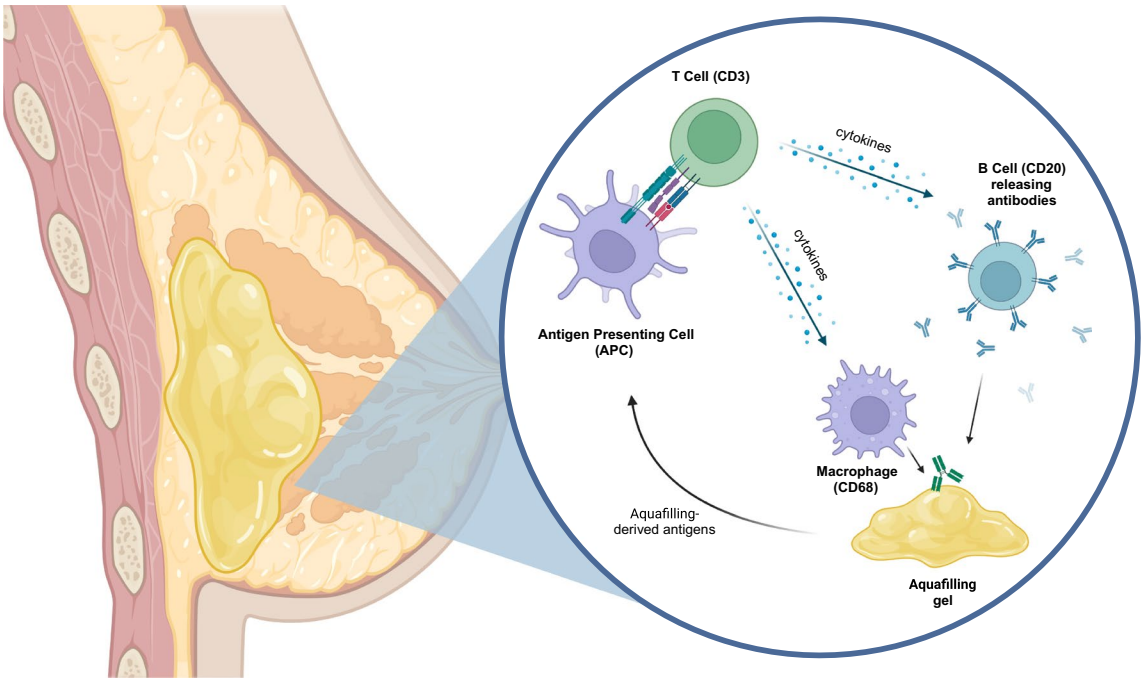

Fig. 3 Probable mechanisms by which CD3, CD20, and CD68 cells are involved in the inflammatory process in the gel-surrounding tissues. Created using BioRender.com

[6, 12]. However, these histopathological findings may be merely coincidental (cancer development independent of gel interactions). Nevertheless, the potential harmful effect of chronic local inflammation supports the idea of prophylactic intervention.

Eleven patients (4.4%) underwent an Aquafilling gel removal procedure, even though they did not experience any symptoms or complications. These procedures were performed mainly because patients were concerned regarding the safety of the aforementioned filler. The remaining 240 (95.6%) patients were treated when the sequelae had already occurred. This indicates a very low level of awareness among patients about the consequences of Aquafilling injection. Furthermore, surgeons are reluctant to intervene when there are no symptoms present because they are aware of the surgery-related strain for patients.

Imaging methods

The most common imaging method performed on patients after Aquafilling injection was a combination of ultrasonography (USG) and magnetic resonance imaging (MRI). Computed tomography (CT) and MRI alone were also frequently performed. USG alone was rarely used. In some cases, USG and MRI were supported with mammography or elastography. Figure 4 depicts the imaging methods performed in Aquafilling patients.

It seems that MRI combined with USG is the best method for gel migration imaging. MRI is the most accurate measurement and USG, due to its accessibility, is a helpful addition. If MRI is not available, CT can be performed instead. Eight studies reported the use of contrast with MRI and two with CT; nonetheless, there is no need to add contrast to localize the filler. Mammography can be used to exclude calcifications.

Laboratory results

Eight studies described the laboratory results of patients suffering from Aquafilling complications. Six of them reported that laboratory findings (including C-reactive protein (CRP) level, White Blood Cells (WBC) count, and erythrocyte sedimentation rate (ESR)) were within normal range. Surprisingly, CRP and WBC were not elevated even in patients with multiple serious complications such as abscesses or fistula formation.

Elevated CRP levels were observed in two cases; however, one of the patients had a lesser degree of elevation (CRP 3.3 mg/dL), whereas the second patient was described as suffering from a purulent infected breast with HIV coinfection (CRP 24.40 mg/dL) [13, 14].

These findings suggest that laboratory tests such as CRP level, WBC count or erythrocyte sedimentation rate are not useful in confirming Aquafilling complications; however, they may be an indicator of a gel infection or some other underlying comorbidity. Therefore, patients with suspected tissue filler sequelae should be assessed during the diagnostic process.

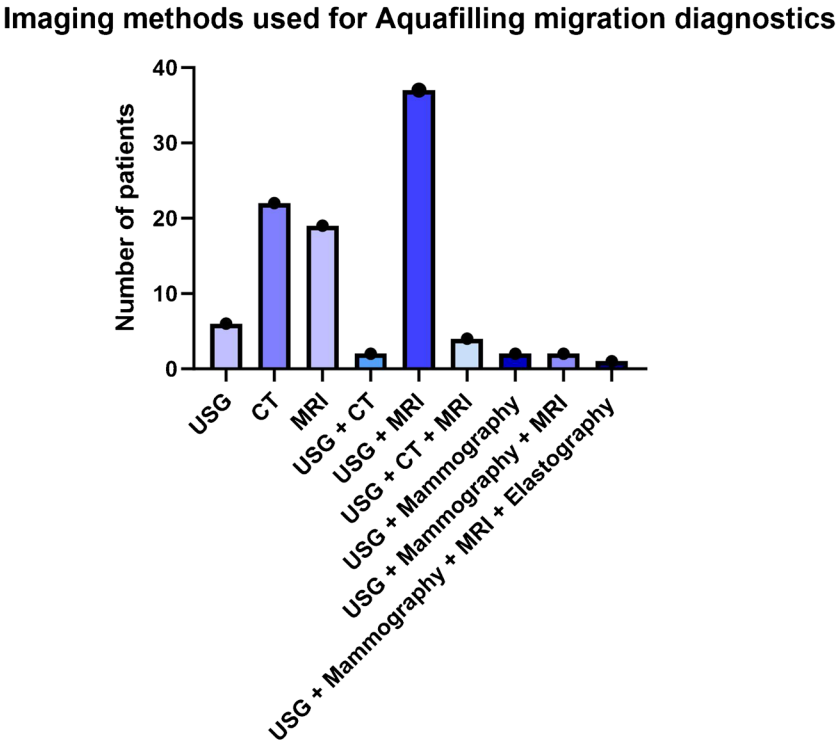

Fig. 4 Imaging methods used for the diagnostic process of Aquafilling-related complications. A combination of Ultrasonography with Magnetic Resonance Imaging seems to be the most favourable

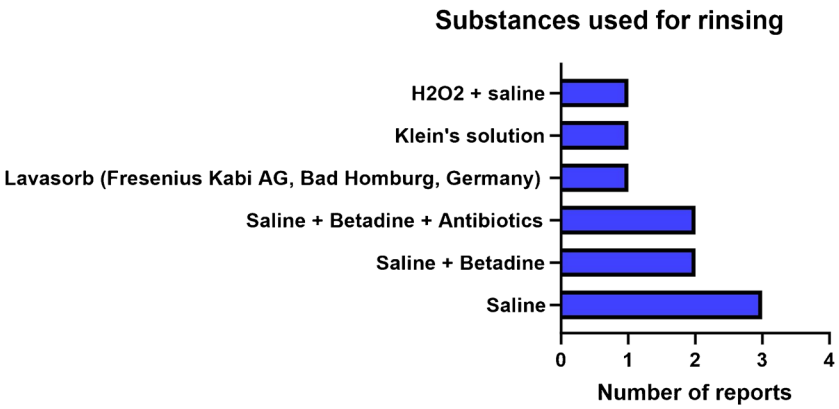

Fig. 5 Substances to be considered for irrigation in Aquafilling removal procedures

Treatment methods

The treatment methods described in the literature rely on four different approaches. The most radical one is mastectomy, which is mainly performed when gel containers coexist with neoplastic lesion [6, 12]. This method has the lowest likelihood of relapse of a gel-related complication; however, it also causes the most severe distress to the patients and has a worse aesthetic outcome compared to the other approaches.

The second method is conservative surgery that relies on massive wound irrigation. It can be performed as a "key-hole surgery" when traditional irrigation is performed through a narrow incision or when various liposuction devices can be used to improve the cleaning efficacy [15]. The fluids used for the irrigation process are shown in Fig. 5.

Another option is conservative treatment, which relies mainly on follow-up combined with anti-inflammatory and analgesic drugs [16]. This method is usually chosen if a patient does not consent to the surgical Aquafilling removal or if the location of the container is challenging to operate (peritoneal cavity infiltration and gel surrounding the liver). This approach is not recommended as only complete gel removal can alleviate symptoms and prevent further complications from developing.

The last method (radical surgery) is a compromise between mastectomy and conservative surgery. It relies on the massive wound irrigation combined with the infiltrated tissue excision [17]. This method allows for comprehensive gel removal with satisfactory aesthetic outcomes. In the case of Aquafilling breast augmentation, an inframammary

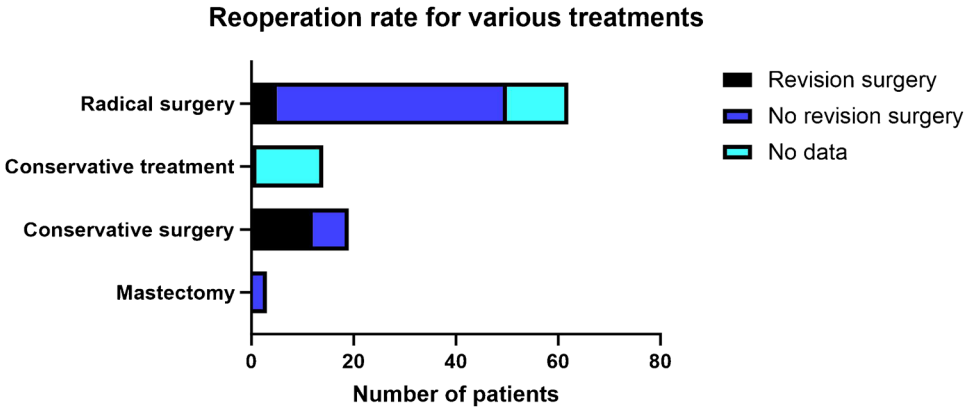

Fig. 6 Reoperation rate for various treatments. The lowest reoperation rate was obtained for the radical surgery and mastectomy, while conservative surgery often required a reoperation. In case of conservative treatment there was usually not enough data regarding the follow-up period

or periareolar incision is usually sufficient. If the infiltration is substantial or gel migration is observed, then additional incisions are required, depending on the gel location.

In the mastectomy cases, no revision surgery was required; however, only three cases of patients undergoing mastectomy after Aquafilling injection have been reported. Conservative surgery had the highest reoperation rate (63% of patients required revision surgery, while 37% did not). After conservative treatment, 7% of patients required surgery; however, there were insufficient follow-up data regarding 93% of patients. It is highly unlikely that they would not have required further surgical intervention, as conservative treatment would not have eliminated the gel. After radical surgery, 8% of patients required a second operation, 73% were cured after primary surgery, and 19% of patients lacked data regarding their follow-up period.

Patients after conservative surgery were significantly more likely to undergo revisional operation than patients after radical surgery (63.16% to 10.00%, respectively, $p < 0.0001$, $OR = 15.43$). It suggests that radical surgery (massive irrigation with infiltrated tissue excision) is superior to conservative surgery (rinsing through a "key hole" or with a liposuction device). The reoperation rate for the various treatment options is shown in Fig. 6. Mastectomy, even though it completely removes the gel, was chosen solely for patients with neoplastic lesions, whereas conservative treatment is only a temporary measure and is usually recommended when surgical intervention was not possible.

Reconstruction

The literature review shows that there is very limited information regarding reconstruction following Aquafilling removal. This suggests a need for further research in this field. One article mentions deep inferior epigastric perforator (DIEP) and implant-based reconstructions following Aquafilling breast augmentation complications [6]. Two articles noted that they performed immediate implant-based breast reconstruction [12, 18]. In a case of tissue necrosis due to filler injection, chest wall skin reconstruction was performed using an integra matrix wound dressing (followed by split thickness skin graft) [14]. Four articles reported on the use of vacuum assisted closure (VAC) after gel excision.

Nine articles reported the absence of reconstruction following the cleansing surgery. This may be caused by the patient's fear of further augmentation following their unpleasant Aquafilling-related experience. Surgeons may also be reluctant to reconstruct the breast immediately due to the unpredictable Aquafilling removal outcome and lack of guidance in the literature. More data are needed with regard to the recommended reconstruction methods, particularly the need for immediate reconstruction versus delayed reconstruction. For instance, implant insertion following an incomplete filler removal may lead to an exacerbation of a prior complication. On the other hand, immediate reconstruction causes less distress to the patient than two consecutive surgeries.

Antibiotic therapy

Eleven articles describe 30 cases of positive culture swabs taken from the gel container. Gierej et al. showed that the tissue filler infection rate was significantly higher in patients who attempted to remove the gel via a needle prior to hospital treatment [17]. They also emphasized that vast heterogeneity of pathogens may indicate infections being caused by numerous injections during removal attempts. The most commonly reported bacteria were *Staphylococcus aureus*; however, *Streptococci, Enterococcus*, and *Pseudomonas aeruginosa* were also found. One article reported *Candida parapsilosis* in the gel-derived culture.

The heterogeneity of pathogens indicates that antibiotics should be administered according to the antibiogram. Nevertheless, ciprofloxacin or clindamycin may be considered if empirical treatment is required; however, further research is needed [8, 17, 19].

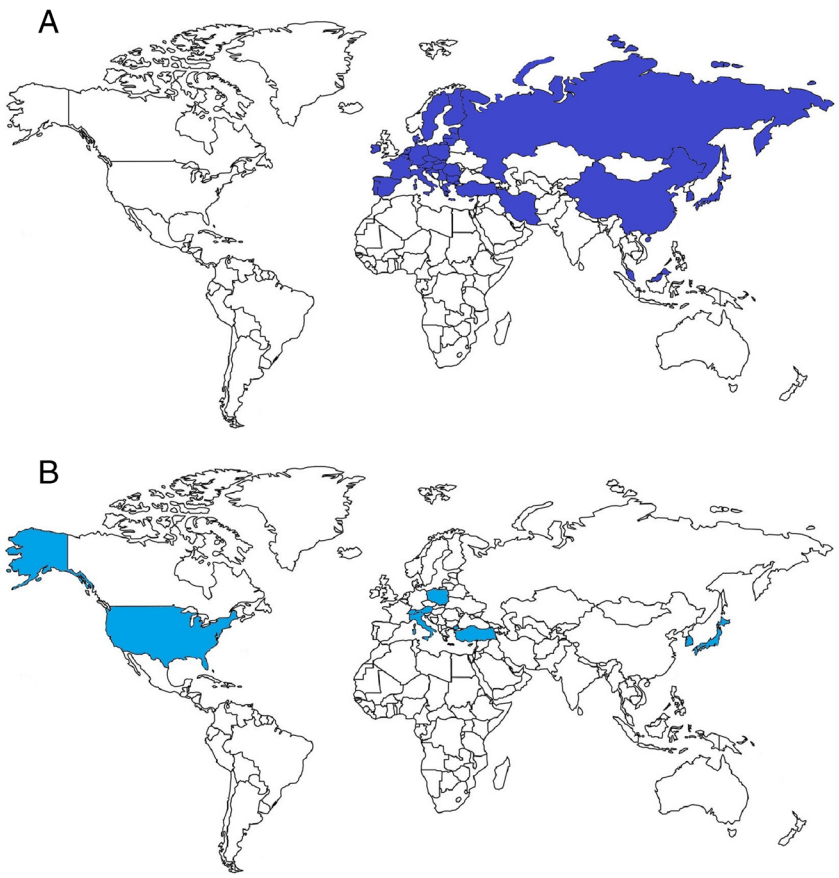

Fig. 7 Prevalence of Aquafilling injections based on the literature (**A**) and places of origin of the research teams studying gel safety (**B**)

Prevalence of Aquafilling injection

Based on the information retrieved from the selected articles, Aquafilling was distributed throughout the European Union, Serbia, Turkey, Japan, South Korea, Malaysia, Russia, China, and Iran [20, 21]. Original articles and case reports describing patients with Aquafilling complications were published by research teams from South Korea (14 articles), Poland (5), Türkey (5), Japan (2), Switzerland (2), Austria/Italy (1), and Türkiye/USA (1). The prevalence of Aquafilling injections is shown in Fig. 7.

Elahi et al. underline that the patients described in their study received tissue filler injection abroad. Subsequently, they were treated by their team in Switzerland [22]. Gierej et al. emphasized that Aquafilling is prohibited in Poland; nevertheless, patients suffering from its complications were encountered [8]. Similarly, in South Korea, Aquafilling is not registered for breast or buttock augmentation; nonetheless, there are numerous cases of complications following these procedures described in the literature [4].

This data shows that Aquafilling complications are not a regional problem. Moreover, patients suffering from gel injection complications may be encountered by physicians not only in the countries where it is being distributed. This leads to the conclusion that knowledge concerning diagnostics and treatment of Aquafilling complications can be useful for physicians around the world.

Conclusions

In the long run, Aquafilling injection may result in a variety of complications. The most common are induration, firmness, pain, and gel migration. It triggers inflammation for which prophylactic removal should be considered. The risk of neoplastic progression following Aquafilling injection requires further research. A combination of magnetic resonance imaging and ultrasonography is recommended as part of the diagnostic process. Elevated CRP, WBC or ESR are not typical for gel complications and indicate possible comorbidities or advanced gel infections. The recommended treatment is a radical surgical approach (massive irrigation with infiltrated tissue excision). There is not enough information in the literature regarding reconstruction, especially regarding immediate reconstruction. Antibiotics should be administered according to the antibiogram, or if empirical treatment is needed, ciprofloxacin or clindamycin can be considered; however, further research is required.

Aquafilling is mainly distributed in Europe and Asia; however, patients suffering from its complications may be encountered far away from the clinic where the substance was injected.

Author contributions Marcin Radziszewski conceived the idea and wrote the manuscript. Łucja Radziszewska and Zuzanna Kaczor collected and analysed the data. Piotr Gierej provided critical feedback and shaped the manuscript.

Funding The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Declarations

Ethics approval Ethics approval is not applicable for this type of study.

Consent to participate Consent to participate is not applicable for this type of study.

Consent to publish Consent to publish is not applicable for this type of study.

Competing interests The authors have no relevant financial or non-financial interest to disclose.

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