Structural Fat Grafting to Improve Outcomes of Vocal Folds’ Fat Augmentation: Long-term Results

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Abstract
Objective. Evaluating the long-term outcomes of vocal fold structural fat grafting.

Study Design. Case series with chart review.

Setting. University hospital.

Subjects and Methods. Seventy-nine dysphonic patients (16-82 years; 55 with unilateral laryngeal paralysis and 24 with vocal fold scarring) underwent vocal fold fat injection. Fat was harvested by low-pressure liposuction and then processed by centrifugation. Refined fat aliquots were placed in the vocal fold and paraglottic space in multiple tunnels to enhance graft neovascularization. All patients were followed for 12 months, 15 for 3 years, and 5 for 10 years with videolaryngostroboscopy, maximal phonation time (MPT) measurement, Voice Handicap Index (VHI) questionnaire, and GRBAS (grade, roughness, breathiness, asthenia, strain) perceptual evaluation. Laryngeal computed tomography (CT) and/or magnetic resonance imaging (MRI) studies were performed in 16 patients 3 to 28 months postoperatively; MRI was repeated in 5 cases 12 to 18 months after the first radiological study.

Results. The voice quality of all patients improved after surgery, and long-term stability was confirmed by MPT, GRBAS, and VHI (P ranging between .004 and <.001). The results achieved 1 year postoperatively remained stable at 3 and 10 years. Videolaryngostroboscopy showed improved glottic closure in all patients despite a limited amount of fat resorption. CT and MRI demonstrated survival of the fat grafts in all of the 16 examined cases. Serial MRI scans showed no change in graft size over time.

Conclusions. The reported clinical and radiological data demonstrate that fat is an effective filler for permanent vocal fold augmentation if the refined micro-aliquots are placed in multiple tunnels.

Keywords
structural fat grafting, dysphonia, glottic incompetence, vocal fold scarring, vocal fold paralysis

Chronic dysphonia is a disabling condition that significantly affects quality of life and can negatively affect social relationships and professional careers. Vocal fold paralysis (VFP) or defects in the multilayered structure of the vocal fold are common causes of dysphonia due to incomplete glottic closure. The etiology of VFP can be idiopathic, traumatic, or, more commonly, iatrogenic. Glottic insufficiency related to a vocal fold soft tissue defect can occur following an ablative surgery for benign or malignant vocal fold lesions; it can also be due to congenital or acquired sulcus vocalis. The inadequate adduction of the vocal folds produces a glottic gap that causes a breathy voice and significant effort during phonation. Patients can experience shortness of breath and vocal fatigue. Voice rehabilitation is often the initial treatment for glottic insufficiency. However, if rehabilitation produces unsatisfactory results, surgical treatment can reestablish glottic competence by augmenting the volume of the affected vocal fold. Glottic closure is necessary to ensure a subglottic pressure adequate to elicit an efficient vibration of the vocal folds and appropriate voice quality. The procedures used to correct glottic insufficiency include the medialization of the vocal fold using an external laterocervical approach or augmentation by injecting the vocal fold with either an implant or autologous tissue. The most commonly used implants

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and biomaterials are polydimethylsiloxane,\textsuperscript{7} hydroxyapatite,\textsuperscript{8} hyaluronic acid,\textsuperscript{9} and micronized dermis.\textsuperscript{10} Implants allow the augmentation of vocal folds on an outpatient basis, under local anesthesia\textsuperscript{11}; however, local and systemic complications can occur, including foreign body reactions, extrusion, and reduced tissue pliability, with possible permanent worsening of dysphonia.\textsuperscript{12} The autologous tissues used are mainly fascia\textsuperscript{13} and fat.\textsuperscript{3,14-16} The use of fat was introduced in the 1990s by Mikaelian et al\textsuperscript{17} and Brandenburg and coworkers.\textsuperscript{18} Due to possible resorption,\textsuperscript{19} fat is still not considered a permanent filler; therefore, implants are widely used, and only a few authors have reported consistent long-term outcomes with fat.\textsuperscript{20}

The aim of the present article was to evaluate the long-term results of vocal fold augmentation using autologous fat harvested at low negative pressure, as well as processed and injected in multiple tunnels for the treatment glottic insufficiency, according to the principles of the structural fat grafting technique.\textsuperscript{21}

**Patients and Methods**

**Patients**

A total of 148 consecutive dysphonic patients underwent vocal fold fat augmentation to correct glottic incompetence between January 2002 and December 2016.

Inclusion criteria were patients aged $\geq$15 years with dysphonia due to either unilateral VFP or vocal fold scarring and previous voice therapy with unsatisfactory results. Exclusion criteria were laryngeal obstruction, main contraindications to general anesthesia, and uncontrolled neurological disease. Patients with incomplete data were excluded from analysis.

The institutional review board of the hospital Policlinico di Milano approved the study protocol.

**Vocal Fold Augmentation Technique**

The procedure was performed by direct microlaryngoscopy under general anesthesia. The fatty tissue was harvested from the lower abdomen with a 10-cc Luer Lock syringe connected to a 2-mm or a 3-mm blunt aspiration cannula. The lipoaspirate was centrifuged at 1200 g for 3 minutes to separate blood to the lower abdomen immediately after surgery and thereafter worn continuously for 10 days.

The diagnostic evaluation was performed preoperatively and at each postoperative assessment.

Videolaryngostroboscopy with a flexible fiberscope or a 70° rigid fiberoptic endoscope allowed us to ascertain the site and severity of the glottic gap, visualize vocal fold vibration abnormalities, plan the injection sites, and objectively assess posttreatment changes.

For perceptual voice evaluation, we used the GRBAS scale,\textsuperscript{24} which subjectively scores the grade of dysphonia (G), roughness (R), breathiness (B), asthenia (A), and strain (S). The voice samples were computer-recorded using a professional microphone (model C 1000 S; AKG Acoustics GmbH, Vienna, Austria) as the subject produced a sustained /a/ while repeating single words and sentences and during conversation. The recordings were subsequently evaluated by 3 experienced independent listeners (2 speech therapists and 1 phoniatrician) and scored in the usual manner ($0$ = normal; $1$ = slight disturbance; $2$ = moderate disturbance; $3$ = severe disturbance). The G, R, and B scores were computed for outcome evaluation. Glottic efficiency was tested...
by measuring the maximum phonation time (MPT) achieved during sustained phonation of the vowel /a/ at a comfortable pitch and loudness; the best of 3 consecutive trials was considered. The Voice Handicap Index (VHI) questionnaire was administered for the self-assessment of perceived voice-related disability. The VHI is a 30-item test with 3 subscales that measure the functional, physical, and emotional aspects of the handicap caused by voice impairment. The subscale scores range from 0 to 40, and the total score ranges from 0 to 120; a higher score indicates a greater degree of disability. A score below 18 is considered within normal limits.

Radiological Study

Sixteen patients volunteered to undergo a radiological study. Computed tomography (CT) and magnetic resonance imaging (MRI) studies of the larynx were obtained in all of the 16 patients 3 to 28 months postoperatively; MRI was repeated in 5 cases 12 to 18 months after the first radiological study (27-42 months postoperatively).

CT studies were performed with a spiral CT scanner (Siemens Somaton Definition; Siemens Medical Systems, Erlangen, Germany) to evaluate pharyngeal and laryngeal structures with a slice thickness of 1.2 mm, without contrast injection. Then reconstruction of the vocal folds was achieved with a multiplanar reconstruction technique with a slice thickness of 3 mm. In CT images, fat tissue appears as black areas.

MRI examinations were acquired with a 1.5 TESLA magnet (Siemens Avanto) with Turbo Spin Echo sequences, T1 and T2 weighted, in axial and coronal planes, with a slice thickness of 3 mm, with no gap, without contrast injection. On MRI, fat tissue appears white in both T1- and T2-weighted images. Vocal fold fat tissue was identified in axial and coronal planes using T1 and T2 images, and bidimensional measurements were performed. For the 5 cases undergoing a second MRI, the same main diameters of fat grafts were measured and compared with the ones obtained on the previous MRI study.

Statistical Analysis

Data were collected by chart reviews of prospectively recruited patients and are presented as mean and their corresponding 95% confidence intervals (CIs). The exact Wilcoxon or marginal homogeneity test (according to the variable type) was used to compare the data before and after surgery. A general linear model for repeated measures was used to investigate changes from baseline in the primary outcome variables (MPT, GRB, and VHI) 3, 12, and 36 months after surgery and to evaluate the impact of the patient’s age and the type of dysphonia (paralytic or nonparalytic) on these variables. Two-sided exact tests were used, and P values less than .05 were considered significant. All of the statistical values were calculated using the Statistical Package for the Social Sciences 20.0 for Windows software package (SPSS, Inc, an IBM Company, Chicago, Illinois).

Results

Seventy-nine (48.1% males; mean age, 49.2 years; 95% CI, 45.9-52.6 years) of 148 patients completed follow-up at 1, 3, and 12 months postoperatively. Among these, 55 (45.4% males; mean age, 51.7 years) were affected by unilateral VFP, with a disease duration of 5 months to 48 years (median, 1.7 years; 95% CI, 4.86-12.41 years; 2 patients had a disease duration of only <10 months, and both at follow-up showed a permanent paralysis), and 24 (54.2% males; mean age, 43.6 years) had soft tissue defects of the vocal folds that were either congenital (sulcus vocalis; 12 cases) or acquired due to sequelae of laryngeal fracture (2), excision of vocal fold malignancies (4), or benign lesions (6). In patients with acquired lesions, the disease duration ranged from 1 to 25 years (median, 3.5 years). Thirteen patients (17.6%) with severe dysphonia—8 with unilateral VFP and 5 with vocal fold soft tissue defects—underwent 1 additional session of fat grafting because the improvement obtained 12 months after the first operation was not fully satisfactory. Eleven patients (13.9%) were followed for 3 years and 5 of these patients for 10 years.

All of the 79 patients tolerated well the procedure and showed no signs of respiratory distress following surgery. Neither donor nor recipient site complications were observed: in particular, there was no hematoma, and only minimal bruises were detected on the abdomen.

Voice quality improved soon after surgery in all cases. Videolaryngostroboscopy showed some degree of resorption in the first 3 to 4 weeks after surgery; nevertheless, a stable improvement in vocal fold closure during phonation occurred in all patients. Figures 1 and 2 demonstrate the
long-term augmentation achieved in 2 of the treated patients.

The long-term stability of voice results was confirmed by MPT, GRBAS scale, and VHI (Table 1). An analysis of variance (ANOVA) revealed that MPT (P < .001), VHI (P < .001), grade of dysphonia (P < .001), roughness (P = .004), and breathiness (P < .001) of the patients’ voice significantly improved regardless of the patient’s age or type of dysphonia.

MPT significantly improved between the preoperative assessment and 3 months after the surgery (P < .001) and continued to improve until 12 months (P = .035) (Table 1 and Figure 3A). VHI, instead, improved between the preoperative evaluation and 3 months postoperatively (P < .001) and remained stable over time (Table 1 and Figure 3B). Similarly, the grade of dysphonia, roughness, and breathiness improved significantly 3 months after the surgery (P < .001 for all the variables) and then remained stable (Table 2). In 16 (20.2%) patients (15 VFP and 1 soft tissue defect), postoperative voice quality reached a score of zero (normality) for the perceptual parameters of the GRBAS scale.

Table 2 shows the results obtained in the 13 patients who underwent an additional session of fat grafting. All the variables significantly (P ranging between .005 and .027) improved after the first surgical procedure and then remained stable over time (Table 2 and Figure 4A,B). Indeed, at the end of follow-up, all the parameters (except for roughness) were statistically improved (P for MPT = .027; P for VHI = .016; P for the grade of dysphonia = .015; and P for the grade of breathiness <.001).

Table 3 reports the results obtained in 11 patients who were followed for 3 years (mean age, 48.5 years; 95% CI, 35.6-61.3 years). In this subgroup, MPT, VHI, and grade of dysphonia significantly improved after 12 months (P ranging between .018 and .039) and plateaued thereafter (Table 3 and Figure 5A,B). Roughness and breathiness had a positive trend over time, but significance was not reached due to the heterogeneity of this small subgroup. The 5 patients who were reassessed 10 years after surgery had stable results. The youngest female patient and a 64-year-old male patient experienced further amelioration over time, and both had normal MPT, VHI, and GRB values. The oldest patient, aged 77 years at the 10-year postoperative reassessment, experienced a slight decline in outcomes due to voice aging.

The radiological follow-up by CT and MRI demonstrated the persistence of the fat grafts in all of the 16 patients, in 20 of 22 injected vocal folds; an example is shown in Figure 6. Further serial MRI scans obtained in 5 patients

### Table 1. Results of the 79 Patients Completing the 12-Month Follow-up.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Preoperatively, Mean (95% CI)</th>
<th>3 Months Postoperatively, Mean (95% CI)</th>
<th>12 Months Postoperatively, Mean (95% CI)</th>
<th>Preoperatively vs 3 Months Postoperatively, P Value</th>
<th>3 vs 12 Months Postoperatively, P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPT, s</td>
<td>7.9 (6.8-9.0)</td>
<td>12.2 (10.1-14.2)</td>
<td>13.6 (10.3-16.9)</td>
<td>&lt;.001</td>
<td>.035</td>
</tr>
<tr>
<td>VHI</td>
<td>64.0 (58.4-69.6)</td>
<td>32.4 (26.2-38.6)</td>
<td>34.5 (23.9-45.0)</td>
<td>&lt;.001</td>
<td>NS</td>
</tr>
<tr>
<td>Grade of dysphonia</td>
<td>2.2 (2.1-2.4)</td>
<td>0.8 (0.6-0.9)</td>
<td>0.9 (0.6-1.2)</td>
<td>&lt;.001</td>
<td>NS</td>
</tr>
<tr>
<td>Roughness</td>
<td>1.1 (0.8-1.3)</td>
<td>0.4 (0.3-0.5)</td>
<td>0.4 (0.1-0.7)</td>
<td>&lt;.001</td>
<td>NS</td>
</tr>
<tr>
<td>Breathiness</td>
<td>1.8 (1.6-2.0)</td>
<td>0.4 (0.2-0.5)</td>
<td>0.5 (0.2-0.8)</td>
<td>&lt;.001</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; MPT, maximal phonation time; NS, nonsignificant; VHI, Voice Handicap Index.

Figure 3. Maximum phonation time (MPT, A) and Voice Handicap Index (VHI, B) scores for the 79 patients before fat grafting and 3 and 12 months after surgery.
12 to 18 months after the first radiological study (27-42 months postoperatively) showed no change in graft size over time (Figure 7).

**Discussion and Conclusion**

The results of this long-term follow-up study confirm our previous short-term findings in patients undergoing vocal fold fat grafting and support that the described technical details can ensure long-term voice improvement. Most of our patients were affected by longstanding severe dysphonia; nevertheless, the disease duration did not influence the outcome.

Videolaryngostroboscopy allowed us to assess the improvement in glottic closure and proved the stability of the grafts over time (Figures 1-2). It is well known that synkinetic recovery of muscle tone and trophism can play a significant role in phonatory improvement in laryngeal hemiplegia. In our series, synkinesis might be a confounding factor for a limited number of cases, considering that the median disease duration for the 55 patients affected by unilateral VFP was 1.7 years. The impact of aberrant reinnervation on our outcomes might have been clarified by electromyography, which was not available for our patients; this represents a limit of our study. A further possible limit of our study is related to the dropout of 69 patients not completing the 12-month follow-up period, which is due to the fact that many of our patients are living far from our region. Prior to statistical analysis, we decided to exclude all patients with incomplete follow-up data; nevertheless, anecdotal results obtained through phone follow-up suggested that these patients did as well as the 79 patients included in the study. Therefore, we think that dropouts do not represent a bias in our study design and results.

The voice perceptual evaluation demonstrated that the grade of dysphonia, breathiness, and roughness significantly ameliorated 3 months after the surgery and remained stable 12 months postoperatively. Furthermore, normal values of the perceptual parameters were achieved in 30% of the patients with VFP and in 1 patient with scarred vocal folds. The MPT measurements objectively demonstrated that glottic closure was more efficient and that the amount of air that escaped through the vocal folds on phonation was significantly reduced. MPT is considered the most basic and simple way to assess the efficiency of glottic closure, as the consumption of air during phonation is inversely proportional to the duration of the MPT. We also investigated

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**Table 2. Results of the 13 Patients Undergoing Second Surgery.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Preoperatively, Mean (95% CI)</th>
<th>After the First Surgery, Mean (95% CI)</th>
<th>After the Second Surgery, Mean (95% CI)</th>
<th>Preoperatively vs after First Surgery, P Value</th>
<th>After First Surgery vs after Second Surgery, P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPT, s</td>
<td>7.8 (5.4-10.3)</td>
<td>11.0 (6.7-15.3)</td>
<td>10.5 (4.9-16.2)</td>
<td>.025</td>
<td>NS</td>
</tr>
<tr>
<td>VHI</td>
<td>72.1 (56.2-88.0)</td>
<td>58.9 (43.2-74.6)</td>
<td>45.0 (26.3-63.7)</td>
<td>.008</td>
<td>NS</td>
</tr>
<tr>
<td>Grade of dysphonia</td>
<td>2.3 (2.0-2.6)</td>
<td>1.7 (1.3-2.0)</td>
<td>1.3 (0.8-1.9)</td>
<td>.009</td>
<td>NS</td>
</tr>
<tr>
<td>Roughness</td>
<td>1.5 (0.9-2.0)</td>
<td>0.7 (0.2-1.1)</td>
<td>1.0 (0.5-1.5)</td>
<td>.005</td>
<td>NS</td>
</tr>
<tr>
<td>Breathiness</td>
<td>2.1 (1.8-2.4)</td>
<td>0.9 (0.1-1.7)</td>
<td>0.7 (0.1-1.3)</td>
<td>.027</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; MPT, maximal phonation time; NS, nonsignificant; VHI, Voice Handicap Index.
the impact of the voice disorder on the patient’s quality of life. The results of the VHI questionnaire proved that the fat graft had a favorable impact on social and emotional life and reduced the physical effort required for phonation. Our results were consistent in the 79 cases followed for 12 months and in the subgroup of 11 patients who were available at follow-up for 36 months. The stability of the achieved results in the 5 patients followed for 10 years further confirms the effectiveness of fat augmentation in permanently ameliorating voice quality. The resorption of the graft, one of the main concerns about the long-term outcomes, was not clinically relevant. It has been demonstrated that to optimize the outcomes and minimize the resorption rate, numerous technical details in each step of fat transfer are crucial.22

Harvesting should be done at low negative pressure by a small-diameter blunt cannula to avoid damage to fragile adipocytes. Placement of micro aliquots of fat parcels, according to the spaghetti-like technique, is recommended.22 Enhancing the contact between the injected fat parcels and the host tissue may avoid fat necrosis, fibrosis, and oil cysts formation.23 To avoid bolus injection in a single site, we performed multiple and multilayered placements in both the vocal fold and paraglottic space. Injecting at multiple entry points may also favor drainage of the residual liquid component of the lipoaspirate: we assumed that the drainage might decompress the graft, facilitating its survival.

The space available for hosting fat into the vocal fold is limited for anatomical reasons; thus, to further reduce the closure gap between the 2 folds, we placed parcels of fat also in the contralateral healthy side. An excess of fat grafted in the paralyzed fold would result in necrosis, resorption, and loss of volume; conversely, injecting also the mobile contralateral fold in our experience can consistently enhance glottic closure. The

**Figure 5.** Maximum phonation time (MPT, A) and Voice Handicap Index (VHI, B) scores for the 11 patients who were followed for 3 years.

**Table 3.** Results of the 11 Patients Followed for 3 Years.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Preoperatively, Mean (95% CI)</th>
<th>Postoperatively, Mean (95% CI)</th>
<th>12 Months Postoperatively, Mean (95% CI)</th>
<th>36 Months Postoperatively, Mean (95% CI)</th>
<th>Preoperatively vs 12 Months Postoperatively, P Value</th>
<th>12 vs 36 Months Postoperatively, P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPT, s</td>
<td>5.3 (3.8-6.7)</td>
<td>10.8 (7.8-13.9)</td>
<td>13.0 (9.7-16.2)</td>
<td>.018</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>VHI</td>
<td>57.6 (40.5-74.8)</td>
<td>16.2 (4.7-27.6)</td>
<td>23.4 (9.7-27.2)</td>
<td>.028</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Grade of dysphonia</td>
<td>2.3 (1.8-2.8)</td>
<td>0.7 (0.1-1.2)</td>
<td>0.6 (0.2-1.1)</td>
<td>.039</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Roughness</td>
<td>0.9 (0.2-1.6)</td>
<td>0.3 (0.1-0.9)</td>
<td>0.4 (0.1-0.7)</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Breathiness</td>
<td>1.8 (1.1-2.5)</td>
<td>0.3 (0.1-0.9)</td>
<td>0.5 (0.1-1.0)</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; MPT, maximal phonation time; NS, nonsignificant; VHI, Voice Handicap Index.

**Figure 6.** Same patient as in Figure 2. Left: preoperative larynx axial computed tomography scan. Arrow = fracture of thyroid cartilage lamina. Right: 14 months after bilateral fat injection; the arrows indicate the hypodense fat grafts.
amount inserted into the healthy side should be limited, to avoid the risk of respiratory obstruction. Nevertheless, none of our patients experienced postoperative dyspnea.

Fat has viscoelastic properties that are similar to those of the lamina propria; thus, it can be an ideal material for augmenting the vocal fold and for restoring its gliding tissue. Since the 1990s, fat has been used for vocal fold augmentation but has often been considered a temporary filler; consequently, implants are widely used. Potential drawbacks of the implants are well known and extensively reported in the literature. Fat is an autologous material, readily available at no cost, and our results demonstrate that fat grafting, performed according to the lipostructure technique, can effectively treat glottic insufficiency. Thirteen patients in our series (17.6%) required a second fat injection; all were affected by severe glottic incompetence and/or severe scarring of both vocal folds. Indeed, they benefited from the first fat grafting but achieved further significant improvement with the second one. In the informed consent, we specify the possibility of a second session of fat grafting to optimize the result.

Despite laryngoscopic evidence that the transplanted fat underwent partial resorption during the first few weeks following the surgery, the radiological evaluation clearly showed long-term survival of the grafted fat in all 16 patients undergoing MRI and/or CT, in agreement with the reports of other authors. In the 5 patients undergoing the serial MRI, no change in graft volume was detected in comparison with the first imaging assessment. To our knowledge, this is the first study demonstrating vocal fold fat graft stability by means of serial MRI.

The ongoing research about the cellular components of adipose tissue has demonstrated the high concentration of multipotent mesenchymal stem cells in the stromal vascular fraction and has shown that centrifugation can concentrate stem cells and angiogenic growth factors in the refined fat grafts. There is evidence that a higher content of stem cells and growth factors may enhance survival of the transplanted fat in experimental and clinical settings. Stem cells, capable of self-renewal and differentiation into multiple cellular lineages, might play an important role in regenerative processes after fat transplantation. A future clinical use of isolated and expanded adipose-derived mesenchymal stem cells and of growth factors might be postulated for enhancing the results obtained so far, especially in cases of severe glottic incompetence.

In conclusion, the described technique of mini-invasive autologous fat handling, processing, and injecting in multiple layers has proved a reliable procedure to achieve long-term voice improvement in the treatment of glottic incompetence. Fat tissue may play a dual role both as a filler and as a regenerative mean.

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Author Contributions
Giovanna Cantarella, design of the work, manuscript drafting, performing surgeries, patient follow-up; Riccardo F. Mazzola, design of the work, manuscript drafting and revision, participation in surgeries; Michele Gaffuri, data acquisition and analysis, participation in drafting and revising the manuscript; Elisabetta Iofrida, data acquisition and analysis, participation in surgeries, revision of statistical data and revision of the manuscript; Pietro Biondetti, performing and reviewing radiological exams, drafting radiological description, critical revision of the manuscript; Laura


