Journal of Clinical and Translational Research 2024; 10(2): 151-158

Journal of Clinical and Translational Research

Journal homepage: http://www.jctres.com/en/home

ORIGINAL ARTICLE

Chances and challenges of combined antegrade and retrograde endoscopic recanalization of complete hypopharyngoesophageal obliteration: a case series

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ARTICLE INFO

Article history:
Received: 02 October, 2023
Accepted: 26 October, 2023
Published Online: March 28, 2024

Keywords:
Hypopharynx obstruction
Rendezvous endoscopic recanalization
Gastrostomy
Oropharyngeal carcinoma
Deglutition
Deglutition disorder

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Abstract

Background: Complete hypopharyngeal obliteration is a serious problem after radiochemotherapy. Data on rendezvous techniques using percutaneous retrograde endoscopy through the gastrostomy channel and antegrade laryngoscopy are limited with a possible bias on positive results.
Aim: This study aimed to review the clinical success, challenges, complications, and failure rates of this technique.
Methods: We prospectively collected data on endoscopic recanalization techniques, subsequent bougienages, adverse events, and final outcomes in seven patients.
Results: Recanalization was technically successful in all patients. However, normal food intake was achieved in only two patients, with one of them under ongoing bougienage. Additive treatment was needed in all patients, including microsurgical scar excision, temporary stent application, argon plasma coagulation, and surgical fistula closure. Salvage laryngopharyngectomy had to be performed in two of the seven patients. Preexisting hypopharyngo-tracheal fistula and therapy-induced fistula represent a technically demanding obstacle, necessitating endoscopic stenting and surgical closure.
Conclusion: Endoscopic recanalization of esophageal obliterations is feasible, although technically demanding. The clinical success rate for long-term normalization of oral food intake is, however, low. Prospective data collection in a larger cohort is urgently needed.
Relevance for Patients: Patients should be informed about the possibility of long-term follow-up treatments and the low clinical success rate of endoscopic recanalization by the rendezvous technique, as well as other alternative approaches while making the decision to accept the treatment.

1. Introduction

Hypopharyngoesophageal strictures occur in approximately 3% of patients after radiotherapy for head and neck cancers, squamous cell carcinomas of the upper esophagus, and laryngeal or oropharyngeal cancers [1,2]. A radiation dose >45 – 60 Gy is a risk factor for stricture formation [1,3]. Complete esophageal obliteration has been reported in 23 – 50% of preselected patients with radiation-induced esophageal strictures [2,4]. The most common site for radiation-induced stenosis is the post-cricoid or cricopharyngeal region [5]. In contrast to subtotal esophageal stenosis, which can be easily treated by endoscopic bougienage, complete obstruction of the lumen usually requires alternative approaches, such as surgical revision, which is a complex and difficult procedure in the pretreated proximal esophagus [3,6].

DOI: https://doi.org/10.36922/jctr.23.00116

Although some authors advocate surgical reconstruction for complete esophageal obstruction [3,7], peroral and transgastric-retrograde rendezvous has been reported for recanalization of subtotal [8-11] and complete esophageal obstruction in single cases and case series [5,11-19] with a high technical and clinical success rate. However, a positive publication bias should be considered when assessing this technique. Patients with cancers of the hypopharynx are at considerable risk for secondary malignancies of the esophagus [20]. Therefore, re-establishment of the pharyngoesophageal passage will not only allow swallowing of saliva or even restore oral nourishment to improve the quality of life but will also enable endoscopic surveillance in these patients.

Here, we report a case series of seven technically successful recanalizations of complete pharyngoesophageal obstruction after radiotherapy by a transgastric-retrograde approach under transillumination, fluoroscopic, and endoscopic guidance.

2. Methods

2.1. Patients

Seven patients eligible for the combined antegrade and retrograde recanalization treatment presented with complete esophageal obliteration, which was confirmed by upper endoscopy. All patients gave their written informed consent for the treatment and the publication of their data.

2.2. Procedures

For recanalization of the upper esophageal entry, we performed a rendezvous technique: after percutaneous endoscopic gastrostomy (PEG) removal, the PEG channel was dilated to 8 mm (CRE PRO Wireguided Balloon Dilatation Catheter, Boston Scientific, Cork, Ireland), and a slim gastroscope (GIF XP160, 5.9 mm, Olympus, Hamburg, Germany) was propagated into the stomach and retrograded into the esophagus up to the distal end of the obliteration. Simultaneous transoral endoscopy under fluoroscopy allowed us to measure the length of the obliteration. After endoscopy, the gastrostomy was kept open by a G-tube (Nutricia Flocare Gastrostomy tube, 14 Ch). On the following day (in some cases within the same procedure), antegrade rigid pharyngoscopy and simultaneous retrograde esophagoscopy through the PEG channel were performed under general anesthesia. Under fluoroscopic, transillumination, and retrograde endoscopic guidance, the proximal blind end of the esophagus was punctured from the hypopharynx with a 1.9 mm straightened needle (Provox Vega Puncture Set, Atos Medical GmbH, Troisdorf, Germany) or with the trocar needle of the PEG set in the following cases after cutting the butterfly flanks to allow passage through the pharyngoscope (Freka PEG Set Gastric FR15, Fresenius Kabi AG, Bad Homburg, Germany). A guidewire was advanced through the needle into the esophagus and grasped with forceps via the gastroscope. The obliteration was reopened either with an endoscopic ring cutter (ring knife model Prof. Dr. U. Will, 1.8 mm, MTW, Wesel, Germany) or a biliary dilation catheter (Cook Medical, Ireland) under intravenous antibiotic coverage with clindamycin or cefuroxime in combination with metronidazole. Subsequently, the opened channel was dilated (2 – 9 mm), and a nasogastric feeding tube was inserted to guide further bougienages.

2.3. Data collection

Data concerning oncological pretreatment, duration, and symptoms of esophageal obliteration were retrospectively collected from the patient´s file. Data on clinical symptoms at presentation, diagnostic work-up, recanalization procedure, bougienage treatments, complications, symptom development, and final outcomes were prospectively collected during each visit.

3. Results

The clinical background of patients with oncologic details and demographic data are listed in detail in Table 1. The mean and median age was 64 and 70 years, respectively. Most patients (71%) were male. All but one patient received radiochemotherapy for their initial oncological treatment. In all patients, a complete esophageal obliteration occurred with complete aphagia, which was verified by a computed tomography scan, lack of contrast media passage, and upper endoscopy. The mean and median length of obliteration was 16.8 and 20 mm, respectively. Details of the recanalization procedure are given in Table 2, and the standard procedure is depicted in Figure 1. The technical success rate of the recanalization procedure in all seven patients was 100%.

Periprocedural complications occurred in only one patient where the preparation needle induced the formation of a 15 mm wide soft-tissue pocket of the esophageal lumen adjacent to the left common carotid artery (Figure 2). To facilitate 6 weeks of pocket obturation by granulation, weekly bougienages under antibiotic coverage were carried out only up to 9 mm, and secretion drainage was ensured by wire-guided insertion of a small gastric tube after each bougienage.

After successful recanalization of the obliterated passage, an average of 30.9 (range 12 – 97) bouginages and balloon dilatations were performed on a weekly or biweekly basis to a final mean diameter of 15.3 mm (range 10 – 20 mm). Additive treatment during bouginage was necessary in six of the seven patients (86%); two patients (#1, #5) needed temporary metal stent implantation (fcSEMS) for fistula with final surgical fistula closure (Figure 3A). Due to the COVID-19-induced restrictions of medical care, one patient (#3) omitted routine follow-up, developed another esophageal occlusion, and needed a second recanalization procedure. Three patients (#4, #6, #7) underwent microsurgical scar excision to improve the entry into the recanalized segment (Figure 3B). Three patients (#1, #4, #5) were treated with argon plasma coagulation for enhanced scar formation and granulation tissue in addition to local triamcinolone treatment (Figure 3C).

After the treatment, all patients could at least consume semisolid food and swallow saliva. Two patients (#3, #5, 29%) resumed normal foot intake and remained PEG-independent, with one of them needing ongoing bougienage. Patient #3 was still under repeated bi- to tri-weekly bouginage, while the other patient (#5) had been healthy, reporting no other complications and needing

DOI: https://doi.org/10.36922/jctr.23.00116

Table 1. Patients' characteristics

Parameter	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5	Patient #6	Patient #7
Age (years)	73	70	72	31	59	67	74
Sex	Male	Male	Female	Female	Male	Male	Male
Tumor (histopathology)	Oropharyngeal carcinoma and synchronous supraglottic carcinoma of the larynx (squamous cell carcinoma)	Oropharyngeal carcinoma (squamous cell carcinoma)	Hypopharyngeal carcinoma (squamous cell carcinoma)	Hypopharyngeal carcinoma (squamous cell carcinoma)	Supraglottic carcinoma of the larynx (squamous cell carcinoma)	Glottic carcinoma of the larynx	Carcinoma of the larynx (squamous cell carcinoma)
TNM (UICC)	pT2 pN2c cM0 R1 pT2 pN2a cM0 R0	cT4 cN0 cM0	cT2 cN0 cM0	cT4 cN2b cM0	pT3 pN3b M0	cT3 cN0 cM0	cT3 cN0 cM0
Oncological treatment modalities	Total laryngectomy and partial resection of oropharynx, reconstruction, aRCHT	pRCHT	pRCHT	ICT + pRCHT	Total laryngectomy with neck dissection	Tumor debulking, pRCHT	pRCHT
Additional neoplasia	NCSLC*, pT4 cN2 cM0 (RCHT 45Gy) Skin cancer (squamous cell carcinoma, head/neck) pT1 pNx R0	Prostate cancer, pT3 pN0 R1 (radical prostate resection) Squamous cell cancer esophagus* 20 cm from incisors (RCHT)	NCSLC, cT2 cN2 cM0, synchronic (RCHT)	None	None.	None	None

Abbreviations: NCSLC: Non-small cell lung cancer; RCHT: Radiochemotherapy; TNM: Staging according to T=Primary tumor, N=Lymph node metastases, and M=Distant metastases. UICC: Union International Contre le Cancer (International Union against Cancer).

Table 2. Synopsis of treatment

Parameter	Patient #1	Patient #2	Patient #3	Patient #4	Patient #5	Patient #6	Patient #7
Length of obliteration (mm)	20	8	20	30	5	30	5
Means of recanalization	Ring cutter, ERC-Balloon 7 mm, bougienage 7 mm	Ring cutter, bougienage 5 mm	ERC Dilatator (7F), bougienage 9 mm	ERC Dilatator (10F), bougienage 5 mm	Ring cutter, bougienage 5 mm	EUS cystotome (10F), bouginage 7 mm	ERC Dilatator (6F), bouginage 5 mm
Technical success of recanalization	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Number of bougienages/ balloon dilatations	8/5	18/4	12	50/47	28/11	17/4	7/5
Final diameter (mm)	10	18	15	16	12	16	20
Additional measures	Three fcSEMSs, surgical fistula closure, APC	RCHT for secondary tumor	Reopening due to re-occlusion	Microsurgical scar excision, triamcinolone, APC	fcSEMS, APC, surgical fistula closure, triamcinolone	Microsurgical scar excision	Microsurgical scar excision
Final outcome	Deceased 3 month after last fcSEMS implantation	Laryngectomy rejected by patient, palliative care for osteolytic infection	Normal eating, PEG removed	Salvage laryngopharyngectomy for esophago- tracheal fistula	Bougienage ongoing, PEG-independent	Bougienage ongoing, PEG-dependent	Salvage laryngopharyngectomy

Abbreviations: APC: Argon plasma coagulation; fcSEMS: fully covered self-expanding metal stent; PEG: Percutaneous endoscopic gastrostomy; RCHT: Radiochemotherapy.

no other treatments, for 958 days after her last bougienage. One patient died shortly after recanalization from lung cancer (#1). One patient (#2) was treated with definitive radiochemotherapy for a secondary poorly differentiated esophageal squamous cell cancer, detected 495 days after recanalization. Externally performed radiotherapy overlapped with the initial radiation field, resulting in esophageal wall necrosis with osteomyelitis and spinal metal implantation (Figure 4A). The patient was lost

DOI: https://doi.org/10.36922/jctr.23.00116

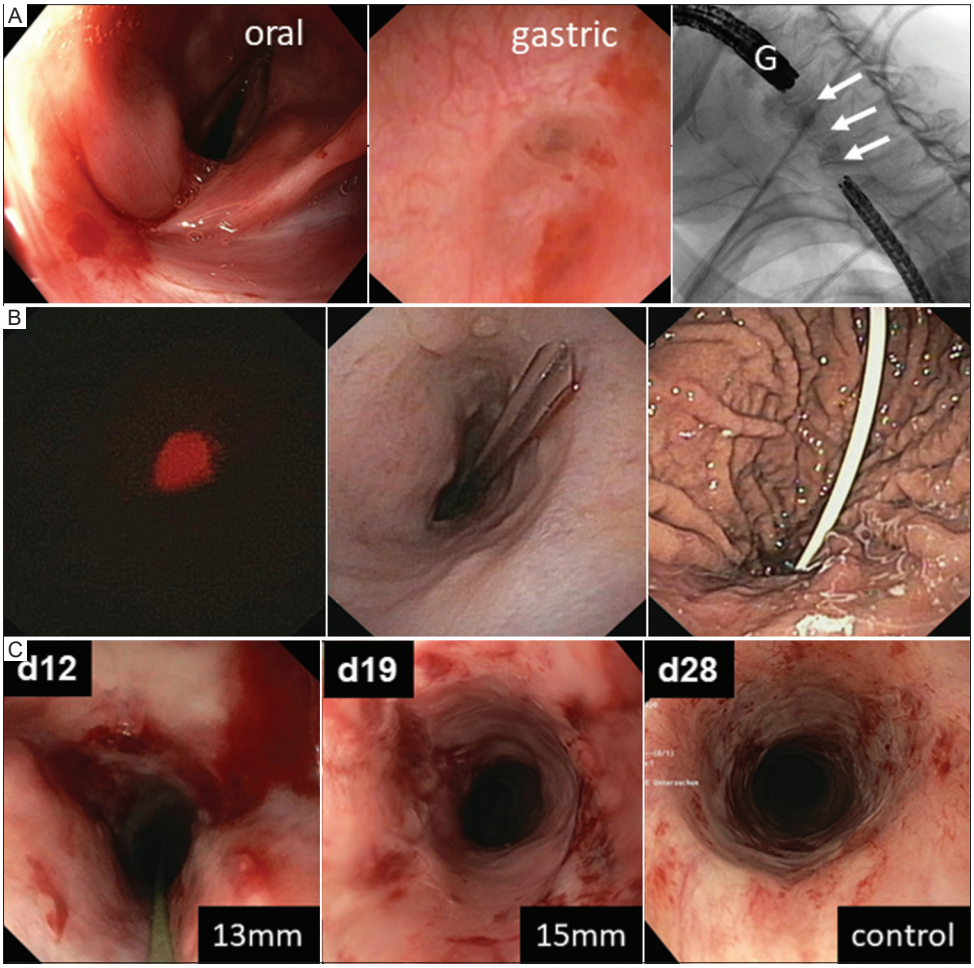

Figure 1. Transgastric-retrograde rendezvous for recanalization of complete esophageal obstruction. (A) Normal gastroscope passage from the oral side was blocked by a complete esophageal obstruction (left). Retrograde esophagoscopy via the percutaneous endoscopic gastrostomy (PEG) channel showed complete obstruction from the gastric side (middle). Simultaneous ante- and retro-grade endoscopy via gastrostomy revealed a 20 mm esophageal occlusion (right, white arrows). (B) Periprocedural transillumination from the antegrade pharyngoscope was detected by retrograde endoscopy via the PEG channel (left). The middle picture shows the per-oral puncture in rendezvous technique and the right picture shows the insertion of a duodenal feeding tube after recanalization of the esophagus. (C) Repeated bougienages at the indicated time points led to a diameter of up to 15 mm.

to follow-up in this palliative setting. Two patients needed salvage laryngopharyngectomy operations: One (#7) decided in favor of an operation after 12 dilatation sessions failed to bring clinical improvement. Another patient (#4) developed a therapy-induced esophago-tracheal fistula (F - fistula, E - esophagus, Figure 4B) and failed to achieve therapeutic success after a long-term bouginage of 97 treatment sessions.

4. Discussion

Recanalization of obliterated esophageal stenosis is a complex multidisciplinary procedure and requires unconventional and individualized solutions to a multitude of problems and complications. Compared with combined ante- and retro-grade recanalization, antegrade endoscopic recanalization results in less complications but involves a longer intervention time [21]. Nevertheless, we are concerned that the previously reported positive clinical results of the procedure might be overstated due to a positive publication bias.

The reported median length of reopened obliterations was 23 mm with a wide range of 2 – 55 mm [18]. The reported primary technical success rates for recanalization of complete obliterations were high: 18/19 patients [18], 5/6 patients [22], 5/5 patients [13], 7/8 patients [19], and 11/11 patients (with 21 procedures) [21]. In our series, all obliterations were successfully recanalized.

There is a high variability in the used techniques and material in our series as well as in published cases. For puncture of the obliterated tissue, endosonography needles have been reported to be challenging due to their high flexibility [13], but have been successfully applied by others [18]. We attempted applying an ultrasound needle (19G, Olympus EZ Shot) in only one patient, but the tractability of the needle was too high for successful puncture, possibly resulting in a pocket formation

DOI: https://doi.org/10.36922/jctr.23.00116

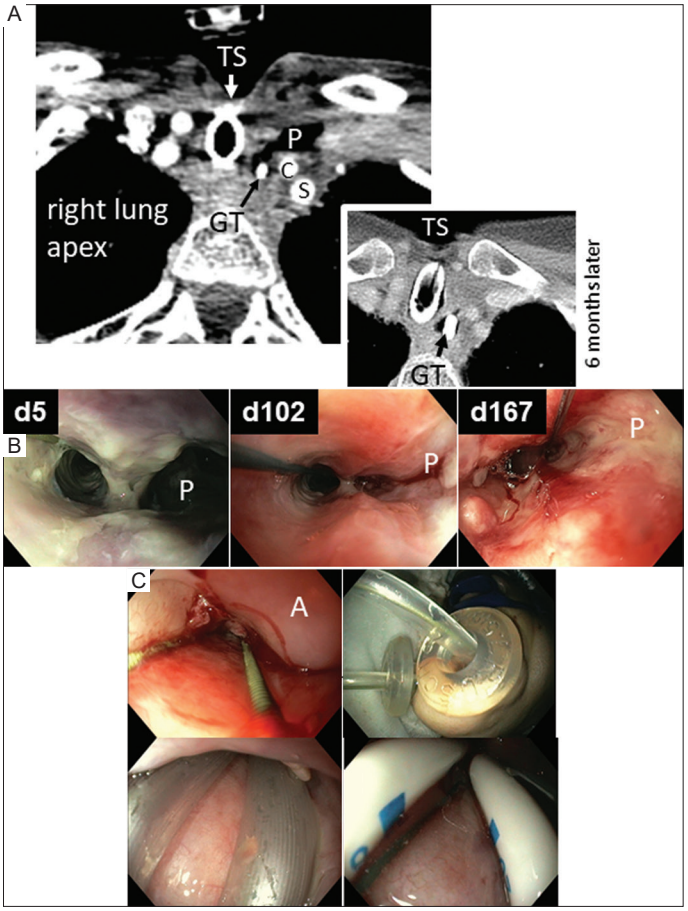

Figure 2. Periprocedural complications. (A) Axial computed tomography plane of the upper thorax aperture demonstrates the soft tissue pocket (P) at the plane of the tracheostomy (TS) adjacent to the common carotid artery (C), left subclavian artery (S) and left lung. The gastric tube (GT) was placed as a placeholder in the esophageal lumen. The inset is an image showing the condition after tissue pocket healing 5 months later. (B) The time-consuming healing of the tissue pocket (P) delayed the progress of bougienages by approximately 100 days. (C) To keep the dilated esophageal entrance next to the arytenoid cartilage (A) open until subsequent bougienage, two guidewires for two gastric tubes were inserted (upper left). Wire-guided and simultaneous insertion of the two gastric tubes had to be assisted by Wendl tubes, one in each nostril (upper right), which splinted the pharynx (lower left) and enabled the simultaneous insertion of two gastric tubes (lower right).

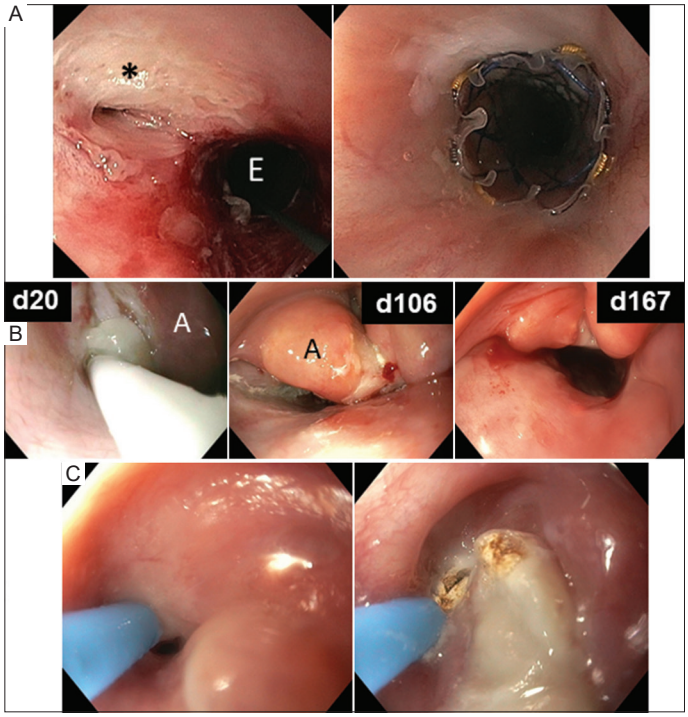

Figure 3. Additive treatments during bouginage. (A) After the eighth bougienage of the recanalized esophagus (E), an esophago-tracheal fistula became evident in patient #1 (*, left) and was endoscopically closed by a fully covered 10 × 100 mm biliary stent (right). (B) To widen the entrance into the recanalization below the arytenoid cartilage, scar tissue was removed by repeated microsurgery, thereby shifting the entrance to the middle (patient #4). (C) Due to recurrent scar formation and granulation tissue cytoreductive, argon plasma coagulation therapy was applied in patient #7.

due to repeated maneuvers with the endosonography needle (patient #4). Needle knife preparation [18] and puncture with the hard end of a wire [22], as well as puncture with a trocar needle from the pharyngeal side [14], as in our cases, have also been reported. Using a stiff needle for puncture from the pharyngeal site offers some advantages regarding maneuverability, especially in obliterations over a longer distance, but still harbors the risk of injuring adjacent and vulnerable structures. Blunt preparation from the oral side under fluoroscopic and endoscopic guidance and puncture of the remaining short segmented soft tissue might be preferable in short-distance occlusions.

Insertion of a feeding tube until repeated bougienages [18] or even the temporal placement of a small-diameter covered metal stent (≤10 mm) [13,14] has been reported as approaches to keeping the pharyngoesophageal passage open after recanalization. However, immediate metal stent insertion did not seem to reduce the necessity of subsequent and repeated bougienages but was associated with a higher abscess formation rate [13]. In this case series, fully covered self-expanding metal stents (fcSEMSs) were used only when fistulas coexisted with the recanalized pharyngoesophageal channel and they did not reduce the need for repeated bougienage. From our experience, the insertion of a gastric tube as a placeholder is highly recommended until the lumen is stable enough to prevent reocclusion. To maintain a functional passage, patients needed up to 32 [18] or even 37 bougienages [4]. In this case series, up to 97 treatment sessions were performed on one patient who did not agree to salvage operation.

An overall complication rate of 11% was reported in the literature for the applied rendezvous technique [15]. It has been reported that mediastinal emphysema [22], pneumothorax [12], pneumomediastinum with periesophageal abscess formation and cervical osteomyelitis, cervical abscess formation [13], and microperforation [19] are mainly managed conservative mode. In

DOI: https://doi.org/10.36922/jctr.23.00116

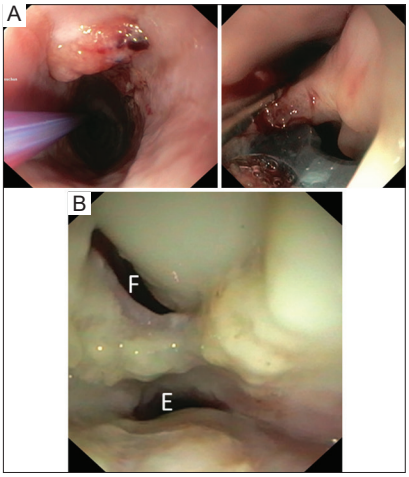

Figure 4. Final outcome. (A) Endoscopic images showing secondary squamous cell carcinoma 3.5 years after initial definitive radiochemotherapy of an oropharyngeal cancer, detected 495 days after recanalization of pharyngo-esophageal obliteration. Radiotherapy resulted in esophageal wall necrosis with an open view of the spine after metal implantation. (B) After 97 bouginages and balloon dilatations, patient #4 developed a therapy-induced esophago-tracheal fistula (F - fistula, E - esophagus).

the seven cases reported in this series, only one direct complication of the recanalization occurred but was managed conservatively.

Despite a high initial technical success rate, the clinical success rate was quite low with a high percentage of additive invasive measures and salvage operations. Although only a minority of reported cases had achieved euphagia without further symptoms (2/19, [18]; 6/24 [15]), most patients could at least consume semisolid food (11/19, [18]; 19/25, [4]; 11/25, [15]) or reported an improvement of their dysphagia score [11]. A recent meta-analysis of 19 studies showed a technical success rate of 89%, but a PEG-free improvement of dysphagia in only 58% [23]. In our cohort, this rate was even lower, measuring only 14%.

Additional adhesions in the hypopharynx and larynx, pronounced scar formation and propulsive dysfunction hamper a normal act of swallowing even after successful treatment of esophageal strictures [24], and approximately 20% – 60% of patients are still dependent on their PEG after recanalization [4,5,15,18,22]. Advanced laryngeal scar formation might hamper the well-coordinated act of swallowing after recanalization. Concomitant intensive swallowing training is essential for clinical success. In addition, in 43% of our patients, microsurgery with scar remodeling was necessary to restore the best possible anatomy to facilitate food passage into the recanalized esophageal entrance. Argon plasma coagulation had been applied in some cases to reduce excessive scars but might have contributed to the esophagotracheal fistula which formed after 97 bouginages in patient #4, resulting in salvage laryngopharyngectomy. Therefore, ablative techniques must be applied with utmost caution.

Tumor surveillance is an important management aspect for hypopharyngeal cancer patients, as they often harbor risk factors for other malignancies [20,25,26]. In one recent case report, localized synchronous squamous cell carcinomas of the esophagus 22 cm from the incisors and hypopharynx were treated by definitive chemoradiotherapy [27]. Definitive radiochemotherapy in our patient was, however, complicated by impaired wound healing, esophageal necrosis, fistula formation, and osteomyelitis.

This study has several limitations. Despite the prospectively collected data, we had no well-defined criteria for which techniques and material to be used, for the time intervals of bougienage and the additive treatments. Long-term follow-up data are needed to demonstrate a long-term benefit even in the two patients with the best result reported in this series. Due to the rarity of this treatment modality, we were only able to provide data on a very small cohort. We propose to prospectively collect data in a multicenter study designed with a predefined instrumental armamentarium, treatment intervals, and outcome parameters.

Applying alternative endoscopic techniques like the per-oral endoscopic tunneling for recanalization of completely obliterated esophageal obstructions has been reported in literature [28-30]. Although this technique holds huge potential, it is very technically demanding, and more investigations are warranted to validate its technical and clinical superiority over the rendezvous procedure.

5. Conclusion

Reestablishment of the pharyngoesophageal passage in patients with complete obstruction after radiochemotherapy can be achieved by a rendezvous technique of antegrade pharyngoscopy and transgastric-retrograde esophagoscopy. However, these patients require highly individualized treatment and follow-up with the need for interdisciplinary, unconventional, and sometimes highly experimental approaches to manage post-interventional obstacles. Despite successful recanalization, complete normalization of the complex act of swallowing can only be expected in a small percentage of patients, and many patients might need repeated interventions over many years. Thus, before implementing the procedure, patients should be informed of the possibility of long-term follow-up interventions. To avoid reocclusion and secondary malignancies, strict and continuous follow-up must be arranged for these patients.

Acknowledgments

The authors would like to thank the patients for their consent to share their clinical course with the scientific community.

Funding

No funds, grants, or other support was received.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Author Contributions

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Data acquisition/clinical care: All authors
Original draft preparation: Ronald Koschny, Gerhard Dyckhoff

DOI: https://doi.org/10.36922/jctr.23.00116

Review and editing: Philippe Federspil, Peter Sauer, Christian Brunner, Peter K. Plinkert, Gerhard Dyckhoff

Ethics Approval and Consent to Participate

Since patient treatment was performed in the context of routine clinical care, prior ethics application was not obtained.

Consent for Publication

Informed consent was obtained from each patient to publish their data anonymously.

Availability of Data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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DOI: https://doi.org/10.36922/jctr.23.00116