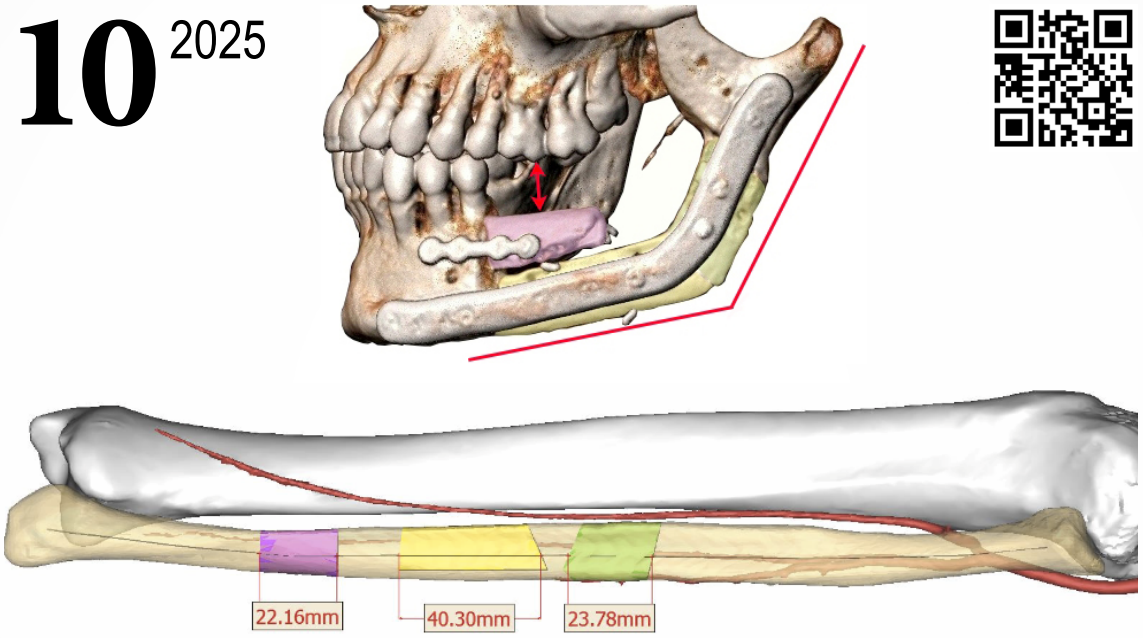
VOLUME 9 • ISSUE 10 OCTOBER 31 • 2025 ISSN 2522-1965

Journal of Diagnostics and Treatment of Oral and Maxillofacial Pathology

10 2025



The cover images indicate the key direction of the journal and highlight an article titled "The 'Beveled One-and-a-Half-Barrel' Fibula Transplant with Virtual Surgical Planning and CT-Guided Implant Surgery for Prosthetic Rehabilitation in Posterior Mandible Defects: A Pictorial Essay" by Olindo MASSARELLI and Silvio Mario MELONI. The article was published in Volume 6, Issue 3.

This is a monthly open access and peer-reviewed publication. This is the first Ukrainian journal dedicated exclusively to oral and maxillofacial surgery, registered in 2016. The Editor in Chief is Oleksii Tymofieiev, Kyiv, Ukraine.

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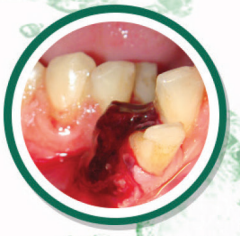
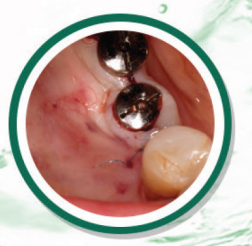
TANTUM VERDE®

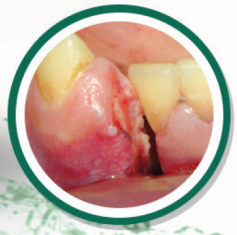
QUICK RELIEF FROM PAIN AND INFLAMMATION IN THE MOUTH AND THROAT[1]

AN INTEGRAL COMPONENT OF THE TREATMENT OF PAIN AND INFLAMMATION IN THE ORAL CAVITY IN 60 COUNTRIES WORLDWIDE![2]

- **JAWS FRACTURES[3]**
- **IMPLANTS PLACEMENT[4]**
- **WOUNDS OF ORAL CAVITY[5]**







Reg. № UA/3920/01/01

LOCAL ANESTHETIC AND ANTI-INFLAMMATORY EFFECT[1]

SUMMARY OF PRODUCT CHARACTERISTICS

NAME OF THE MEDICINAL PRODUCT. Tantum Verde 0.15% mouthwash. QUALITATIVE AND QUANTITATIVE COMPOSITION. Each 100 ml contains: active ingredient: benzydamine hydrochloride 0.15 g (equivalent to 0.134 g of benzydamine). **Therapeutic indications.** Treatment of symptoms such as irritation/inflammation including those associated with pain in the oropharyngeal cavity (e.g. gingivitis, stomatitis and pharyngitis), including those resulting from conservative or extractive dental therapy. **Posology and method of administration.** Pour 15 ml of Tantum Verde mouthwash into the measuring cup, 2-3 times per day, using it either at full concentration or diluted. If diluted, add 15 ml of water to the graduated cup. Do not exceed the recommended dosage. **Contraindications.** Hypersensitivity to benzydamine or to any of the excipient. **PHARMACOLOGICAL PROPERTIES. Pharmacodynamic properties.** Pharmacotherapeutic group: Stomatologic drugs: other agents for local oral treatment, ATC code: A01AD02. Clinical studies demonstrate that benzydamine is effective in relieving suffering from localised irritation of the mouth and pharynx. In addition, benzydamine possesses a moderate local anaesthetic effect. **Pharmacokinetic properties.** Absorption. Absorption through the oropharyngeal mucosa is demonstrated by the presence of measurable quantities of benzydamine in human plasma. These levels are insufficient to produce systemic effects. Distribution. When applied locally, benzydamine has been shown to accumulate in inflamed tissues where it reaches effective concentrations because of its capacity to penetrate the epithelial lining.

Information about medicines. Information for health care professionals for use in professional activities.

1. Інструкція для медичного застосування лікарського засобу Тантум Верде®, розчин для ротової порожнини, РП № UA/3920/01/01, затверджено Наказом Міністерства охорони здоров'я України № 636 від 01.10.2015.
2. http://www.angelinipharma.com/wps/wcm/connect/com/home/Angelini+Pharma+in+the+world/
3. Тимофеев А.А. и др. "Особенности гигиены полости рта для профилактики воспалительных осложнений при переломах нижней челюсти". Современная стоматология 2015;1(75):52–8.
4. 4,5. Tymofieiev O.O. et al"Prevention of inflammatory complications upon surgeries in maxillofacial region". J Diagn Treat Oral Maxillofac Pathol. 2017;1:105–12.

Clinical and CT images are courtesy of: Ievgen Fesenko (Department of Oral & Maxillofacial Surgery, PHEI "Kyiv Medical University", Kyiv, Ukraine), Oleg Mastakov ("SCIEDECE—Scientific Center of Dentistry & Ultrasound Surgery" Kyiv, Ukraine)

ANGELINI

04119, Kiev, Melnikova str. 83D, of. 404.
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Dileo FARMA

About the Journal

OCTOBER 2025 • VOLUME 9 • ISSUE 10
www.dtjournal.org

Official Title

Journal of Diagnostics and Treatment of Oral and Maxillofacial Pathology

Official Title in Ukrainian

Журнал діагностики та лікування оральної і щелепно-лицевої патології

Standard Abbreviation: ISO 4

J. Diagn. Treat. Oral Maxillofac. Pathol.

Acronym

JDTOMP

International Standard Serial Number (ISSN)

ISSN 2522-1965 (online)

Aims & Scope

This is a monthly open access and peer-reviewed oral and maxillofacial surgeons. The journal is focused on trauma, microvascular and jaw reconstructive surgery, dental implants, salivary gland tumors/diseases, TMJ lesions, virtual surgical planning, implementation of ultrasonography into the practice of oral and maxillofacial surgeons.

Editorial Board (EB) Composition

- EB shows significant geographic diversity representing 38 opinion leaders from 15 countries: Brazil, Canada, Colombia, Greece, Hong Kong (SAR), India, Indonesia, Israel, Italy, Slovak Republic, Spain, Ukraine, United Arab Emirates, United Kingdom, and United States.
- The majority of the EB Members have a discernible publication history in Scopus, Web of Science, and journals with a high impact factor.
- The publication records of all EB members are consistent with the stated scope and published content of the journal.
- The journal has several full-time professional editors.
- Gender distribution of the editors: 10.53% women (4 persons), 89.47% men (34 persons), 0% non-binary/other, and 0% prefer not to disclose.

Frequency

12 issues a year (since January 2020)

Publishing Model

The *Journal of Diagnostics and Treatment of Oral and Maxillofacial Pathology* is a fully online-only open access and peer-reviewed publication.

Open Access

Types of Peer Review

The journal employs "double blind" and open reviewing.

Article Publishing Charge (APC)

The APC in this journal is 519 Euro ($590 USD) and 259 Euro ($295 USD)(excluding taxes) depending on the article`s type. Details at website: www.dtjournal.org.

Types of Articles Currently Published by the Journal

Editorials/Guest Editorials/Post Scriptum Editorials, Images, Case Reports/Case Series, Original Articles, Review Articles, Discussions, Paper Scans (*synonyms*: Review of Articles, Literature Scan), Book Scans (*synonym*: Book Reviews), Letters to the Editor (*synonym*: Letters), and Viewpoints.

State Registration in the Ministry of Justice of Ukraine

Registration: Jul 28, 2016 (Certificate: КВ № 22251-12151 Р)
Re-registration: May 21, 2019 (Certificate: КВ № 23999-13839 ПР)
Re-registration: Aug 10, 2021 (Certificate: КВ № 24951-14891 ПР).

State Registration in the National Council of Television and Radio Broadcasting of Ukraine

- The journal is registered as print media (Decision of 2024, April 11, No. 1225). The identifier of print media R30-04318.
- The journal is registered as online media (Decision of 2024, April 25, No. 1454). The identifier of online media R40-04708.

Journal is Included in

Encyclopedia of Modern Ukraine, Google Scholar, National Repository of Academic Texts, Register of Scientific Publications of Ukraine (also known as Ukrainian Scientific Periodicals or Register of Scientific Professional Publications of Ukraine), ResearchGate, Scilit, and Vernadsky National Library of Ukraine

Co-Founders

1. Shupyk National Healthcare University of Ukraine (formerly known as Shupyk National Medical Academy of Postgraduate Education).
2. Private Higher Educational Establishment "Kyiv Medical University."
3. OMF Publishing, Limited Liability Company.

Publisher

OMF Publishing, LLC is an academic publishing company.
Address: 13-A Simferopolska Street, office 121, Kyiv 02096, Ukraine.
ROR ID: https://ror.org/017s0zm38.
E-mail: office@omfpublishing.com.
Website: www.omfpublishing.com.

Crossref Membership

OMF Publishing, LLC is a member of Publishers International Linking Association, Inc. which doing business as a Crossref. OMF Publishing`s active membership: From February 2017 to present.

Digital Object Identifier (DOI) of the Journal

10.23999/j.dtomp

Official Journal of the Association

Ukrainian Association for Maxillofacial and Oral Surgeons

Ukrainian Association for Maxillofacial and Oral Surgeons (UAMOS)

Address: 4-A Profesora Pidvysotskoho Street, Kyiv 01103, Ukraine.
Tel., fax: +38 044 528 35 17.
Website: www.uamos.org.

Editorial Board

OCTOBER 2025 • VOLUME 9 • ISSUE 10
www.dtjournal.org

TANTUM VERDE®

INFORMATION LEAFLET
for the medicinal product

Composition:
active substance: **benzydamine hydrochloride**;
100 mL of solution contain benzydamine hydrochloride 0.15 g;
excipients: ethanol 96%, glycerol, methyl parahydroxybenzoate (E 218), flavor (menthol), saccharin, sodium hydrocarbonate, Polysorbate 20, Quinoline Yellow (E 104), Patent Blue V (E 131), purified water.

Dosage form. Oromucosal solution.
Basic physical and chemical properties: a clear green liquid with a typical mint flavor.

Pharmacotherapeutic group. Dental preparations. Other agents for local oral treatment.
ATC code: A01A D02.

Pharmacological properties.
Pharmacodynamics.
Benzydamine is a non-steroidal anti-inflammatory drug (NSAID) with analgesic and antiexudative properties.

Clinical studies have shown that benzydamine is effective in the relief of symptoms accompanying localized irritation conditions of the oral cavity and pharynx. Moreover, benzydamine has anti-inflammatory and local analgesic properties, and also exerts a local anesthetic effect on the oral mucosa.

Pharmacokinetics.
Absorption through the oral and pharyngeal mucosa has been proven by the presence of measurable quantities of benzydamine in human plasma. However, they are insufficient to produce any systemic pharmacological effect. The excretion occurs mainly in urine, mostly as inactive metabolites or conjugated compounds.

When applied locally, benzydamine has been shown to cumulate in inflamed tissues in an effective concentration due to its ability to permeate through the mucous membrane.

Clinical particulars.
Indications.
Symptomatic treatment of oropharyngeal irritation and inflammation; to relieve pain caused by gingivitis, stomatitis, pharyngitis; in dentistry after tooth extraction or as a preventive measure.
Contraindications.
Hypersensitivity to the active substance or to any other ingredients of the product.

Interaction with other medicinal products and other types of interaction.
No drug interaction studies have been performed.

Warnings and precautions.
If sensitivity develops with long-term use, the treatment should be discontinued and a doctor should be consulted to get appropriate treatment.

In some patients, buccal/pharyngeal ulceration may be caused by severe pathological processes. Therefore, the patients, whose symptoms worsen or do not improve within 3 days or who appear feverish or develop other symptoms, should seek advice of a physician or a dentist, as appropriate.

Benzydamine is not recommended for use in patients hypersensitive to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs).

The product can trigger bronchospasm in patients suffering from or with a history of asthma. Such patients should be warned of this.

For athletes: the use of medicinal products containing ethyl alcohol might result in positive antidoping tests considering the limits established by some sports federations.

Use during pregnancy or breast-feeding
No adequate data are currently available on the use of benzydamine in pregnant and breastfeeding women. Excretion of the product into breast milk has not been studied. The findings of animal studies are insufficient to make any conclusions about the effects of this product during pregnancy and lactation.

The potential risk for humans is unknown.

TANTUM VERDE should not be used during pregnancy or breast-feeding.

Effects on reaction time when driving or using machines
When used in recommended doses, the product does not produce any effect on the ability to drive and operate machinery.

Method of administration and doses.
Pour 15 mL of TANTUM VERDE solution from the bottle into the measuring cup and gargle with undiluted or diluted product (15 mL of the measured solution can be diluted with 15 mL of water). Gargle 2 or 3 times daily. Do not exceed the recommended dose.

Children.
The product should not be used in children under 12 years due to a possibility of ingestion of the solution when gargling.

Overdosage.
No overdose has been reported with benzydamine when used locally. However, it is known that benzydamine, when ingested in high doses (hundreds times higher than those possible with this dosage form), especially in children, can cause agitation, convulsions, tremor, nausea, increased sweating, ataxia, and vomiting. Such acute overdose requires immediate gastric lavage, treatment of fluid/salt imbalance, symptomatic treatment, and adequate hydration.

Adverse reactions.
Within each frequency group, the undesirable effects are presented in order of their decreasing seriousness.

Adverse reactions are classified according to their frequency: very common (≥ 1/10); common (≥ 1/100 to <1/10); uncommon (≥ 1/1,000 to <1/100); rare (≥ 1/10,000 to <1/1,000); very rare (<1/10,000); frequency unknown (cannot be estimated from the available data).

Gastrointestinal disorders: rare – burning mouth, dry mouth; *unknown* – oral hypesthesia, nausea, vomiting, tongue edema and discoloration, dysgeusia.

Immune system disorders: rare – hypersensitivity reaction, *unknown* - anaphylactic reaction.

Respiratory, thoracic and mediastinal disorders: very rare –laryngospasm; *unknown* – bronchospasm.

Skin and subcutaneous tissue disorders: uncommon – photosensitivity; *very rare* – angioedema; *unknown* – rash, pruritus, urticaria.

Nervous system disorders: unknown – dizziness, headache.

TANTUM VERDE contains methyl parahydroxybenzoate, which can cause allergic reactions (including delayed-type reactions).

Shelf life. 4 years.

Storage conditions.
Do not store above 25°C. Keep out of reach of children.

Packaging.
120 mL of solution in a bottle with a measuring cup; 1 bottle per cardboard box.

Dispensing category.
Over-the-counter medicinal product.

Manufacturer.
Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A., Italy.

Location of the manufacturer and its business address.
Via Vecchia del Pinocchio, 22 – 60100 Ancona (AN), Italy.

Date of the last revision of the text.
September 26, 2018.

Information leaflet is
APPROVED by
Order of the
Ministry of Health of Ukraine
No. 636 dated 01.10.2015
Registration Certificate
No. UA/3920/01/01

Міністерство юстиції України

Свідоцтво

про державну реєстрацію друкованого засобу масової інформації

Серія КВ № 24951-14891ПР

«Журнал діагностики та лікування оральної і щелепно-лицевої патології»
(назва видання державною мовою)

«Journal of Diagnostics and Treatment of Oral and Maxillofacial Pathology»
(назва видання іншою мовою (мовами))

Вид видання журнал
(газета, журнал, бюлетень, збірник, альманах, календар, дайджест)

Статус видання вітчизняне
(вітчизняне, спільне)

Мова (мови) видання змішаними мовами: українська, англійська

Вид видання за цільовим призначенням наукове, науково-виробниче
(громадсько-політичне, наукове, навчальне, інформаційне, рекламне (понад 40 відсотків обсягу одного номера – реклама), еротичне тощо)

Обсяг, періодичність 23,1 ум. друк. арк., формат А4 (210х297мм), 1 раз на місяць

Сфера розповсюдження та категорія читачів загальнодержавна, зарубіжна
лікарі-стоматологи-хірурги; лікарі ультразвукової діагностики, лікарі-рентгенологи, лікарі-патологоанатоми, студенти, лікарі-інтерни, слухачі, аспіранти, докторанти, наукові, науково-педагогічні та педагогічні працівники закладів вищої освіти та наукових установ

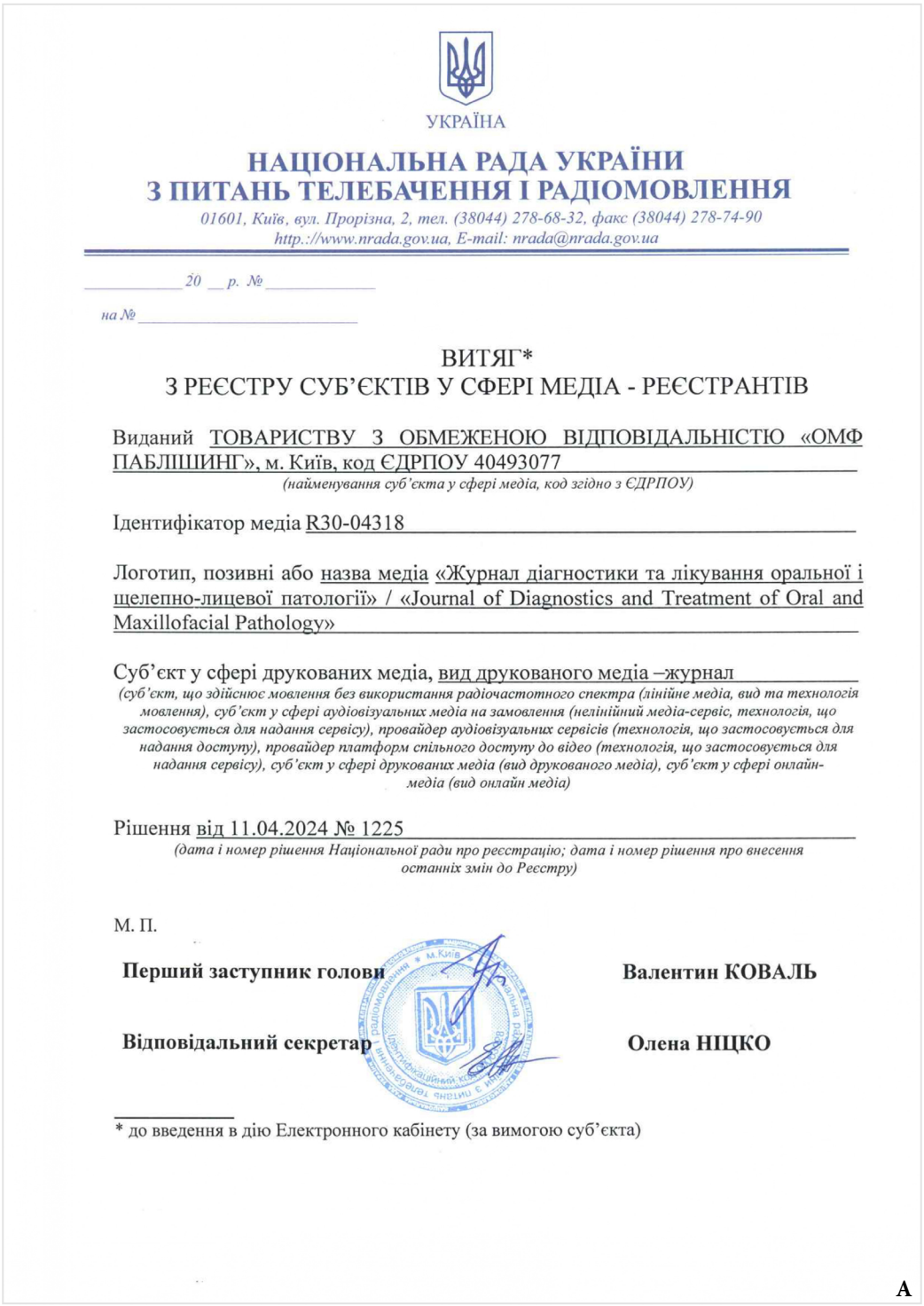
Засновник (співзасновники) Національний університет охорони здоров'я України імені П.Л. Шупика (код за ЄДРПОУ 01896702), Приватний вищий навчальний заклад «Київський медичний університет» (код за ЄДРПОУ 16478809), Товариство з обмеженою відповідальністю «ОМФ ПАБЛІШИНГ» (код за ЄДРПОУ 40493077)

Програмні цілі (основні принципи) або тематична спрямованість журнал присвячений сучасним проблемам діагностики і лікування в хірургічній стоматології та щелепно-лицевій хірургії

Перший заступник Міністра **Євгеній ГОРОВЕЦЬ**

10.08.2021
(дата реєстрації)

FIGURE 1. Certificate of State Re-Registration of the Print Mass Media (journal) in the Ministry of Justice of Ukraine as of 2021. The *Journal* was registered for the first time in 2016 under the title *Diagnostics and Treatment of Oral and Maxillofacial Pathology*. The next re-registration took place in 2019.



УКРАЇНА

НАЦІОНАЛЬНА РАДА УКРАЇНИ
З ПИТАНЬ ТЕЛЕБАЧЕННЯ І РАДІОМОВЛЕННЯ

01601, Київ, вул. Прорізна, 2, тел. (38044) 278-68-32, факс (38044) 278-74-90
http.://www.nrada.gov.ua, E-mail: nrada@nrada.gov.ua

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ВИТЯГ*
З РЕЄСТРУ СУБ'ЄКТІВ У СФЕРІ МЕДІА - РЕЄСТРАНТІВ

Виданий ТОВАРИСТВУ З ОБМЕЖЕНОЮ ВІДПОВІДАЛЬНІСТЮ «ОМФ ПАБЛІШИНГ», м. Київ, код ЄДРПОУ 40493077
(найменування суб'єкта у сфері медіа, код згідно з ЄДРПОУ)

Ідентифікатор медіа R30-04318

Логотип, позивні або назва медіа «Журнал діагностики та лікування оральної і щелепно-лицевої патології» / «Journal of Diagnostics and Treatment of Oral and Maxillofacial Pathology»

Суб'єкт у сфері друкованих медіа, вид друкованого медіа –журнал
(суб'єкт, що здійснює мовлення без використання радіочастотного спектра (лінійне медіа, вид та технологія мовлення), суб'єкт у сфері аудіовізуальних медіа на замовлення (нелінійний медіа-сервіс, технологія, що застосовується для надання сервісу), провайдер аудіовізуальних сервісів (технологія, що застосовується для надання доступу), провайдер платформ спільного доступу до відео (технологія, що застосовується для надання сервісу), суб'єкт у сфері друкованих медіа (вид друкованого медіа), суб'єкт у сфері онлайн-медіа (вид онлайн медіа)

Рішення від 11.04.2024 № 1225
(дата і номер рішення Національної ради про реєстрацію; дата і номер рішення про внесення останніх змін до Реєстру)

М. П.

Перший заступник голови **Валентин КОВАЛЬ**

Відповідальний секретар **Олена НІЦКО**

* до введення в дію Електронного кабінету (за вимогою суб'єкта)

A

FIGURE 2. The *Journal* is registered by the National Council of Television and Radio Broadcasting of Ukraine as print media (**A**) (Decision of April 11, 2024, No. 1225) and online media (**B**) (Decision of April 25, 2024, No. 1454). The identifier of print media is R30-04318 and the identifier of online media is R40-04708. **(Fig 2 continued on next page.)**

УКРАЇНА

НАЦІОНАЛЬНА РАДА УКРАЇНИ
З ПИТАНЬ ТЕЛЕБАЧЕННЯ І РАДІОМОВЛЕННЯ

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ВИТЯГ*
З РЕЄСТРУ СУБ'ЄКТІВ У СФЕРІ МЕДІА - РЕЄСТРАНТІВ

Виданий ТОВАРИСТВУ З ОБМЕЖЕНОЮ ВІДПОВІДАЛЬНІСТЮ «ОМФ ПАБЛІШИНГ», м. Київ, код ЄДРПОУ 40493077
(найменування суб'єкта у сфері медіа, код згідно з ЄДРПОУ)

Ідентифікатор медіа R40-04708

Логотип, позивні або назва медіа «Journal of Diagnostics and Treatment of Oral and Maxillofacial Pathology» / «Журнал діагностики та лікування оральної і щелепно-лицевої патології»

Суб'єкт у сфері онлайн-медіа, вид онлайн-медіа – журнал
(суб'єкт, що здійснює мовлення без використання радіочастотного спектра (лінійне медіа, вид та технологія мовлення), суб'єкт у сфері аудіовізуальних медіа на замовлення (нелінійний медіа-сервіс, технологія, що застосовується для надання сервісу), провайдер аудіовізуальних сервісів (технологія, що застосовується для надання доступу), провайдер платформ спільного доступу до відео (технологія, що застосовується для надання сервісу), суб'єкт у сфері друкованих медіа (вид друкованого медіа), суб'єкт у сфері онлайн-медіа (вид онлайн медіа)

Рішення від 25.04.2024 № 1454
(дата і номер рішення Національної ради про реєстрацію; дата і номер рішення про внесення останніх змін до Реєстру)

М. П.

Перший заступник голови **Валентин КОВАЛЬ**

Відповідальний секретар **Олена НІЦКО**

* до введення в дію Електронного кабінету (за вимогою суб'єкта)

B

FIGURE 2 (continued). The *Journal* is registered by the National Council of Television and Radio Broadcasting of Ukraine as print media (**A**) (Decision of April 11, 2024, No. 1225) and online media (**B**) (Decision of April 25, 2024, No. 1454). The identifier of print media is R30-04318 and the identifier of online media is R40-04708. **(Fig 2 continued on next page.)**

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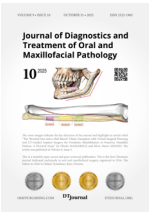

COURTESY

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The images were taken from this article: Massarelli O, Meloni SM. The “beveled one-and-a-half-barrel” fibula transplant with virtual surgical planning and CT-guided implant surgery for prosthetic rehabilitation in posterior mandible defects: a pictorial essay. *J Diagn Treat Oral Maxillofac Pathol* **2022**;6(3):39–59.

https://doi.org/10.23999/j.dtomp.2022.3.3

CASE REPORT

Undiagnosed Factor V Leiden Presenting as Free Flap Thrombosis in Mandibular Reconstruction: A Case Report

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SUMMARY

Microvascular free flap reconstruction remains the gold standard for repairing complex head and neck defects, yet vascular thrombosis continues to pose a serious threat to flap viability. Flap failure is often attributed to technical or local factors; however, the contribution of underlying hypercoagulable states is frequently underrecognized. We present the case of a 71-year-old male with no personal or family history of thrombosis who developed both intraoperative and postoperative arterial and venous thromboses of a fibula free flap used for mandibular reconstruction following extirpation of squamous cell carcinoma. Flap loss led to hematologic evaluation, revealing previously undiagnosed heterozygous Factor V Leiden (FVL). The patient subsequently underwent successful contralateral fibula reconstruction using a modified anticoagulation regimen that included intraoperative heparin boluses and continuous postoperative heparin for therapeutic anticoagulation in intensive care. This case highlights the potential for occult thrombophilia to cause flap failure in the absence of technical error or thrombotic history. It underscores the need for individualized risk assessment and tailored perioperative planning in complex microsurgical reconstruction when there is clinical suspicion of systemic coagulopathic dyscrasia.

KEY WORDS

Factor V, thrombophilia, free tissue flaps, myocutaneous flap, surgical flaps, head and neck neoplasms, squamous cell carcinoma of head and neck, neck dissection, mandibular reconstruction, mandibular neoplasms, venous thrombosis, arterial thrombosis, anticoagulants, plastic surgery procedures, oral surgical procedures, perioperative care, aspirin, heparin, case reports, review

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Conflict of Interest Disclosures: None of the authors have any relevant financial relationship(s) with a commercial interest. The authors declare no financial conflict of interest.

Article type: Case report.

Please cite this article as: Thornton B, Rothman N, Patel K, Kase MT, Morlandt AB, Ponto J. Undiagnosed factor V Leiden presenting as free flap thrombosis in mandibular reconstruction: A case report. J Diagn Treat Oral Maxillofac Pathol. 2025 Oct;9(10):100311.

Manuscript received 30 July 2025
Accepted 30 September 2025
Available online 01 October 2025

https://doi.org/10.23999/j.dtomp.2025.10.100311

INTRODUCTION

Microvascular free flap reconstruction is the standard of care for repairing complex head and neck defects following oncologic resection, with reported success rates of 90–95% [1-3]. Despite these favorable outcomes, flap failure due to vascular thrombosis—most commonly venous—remains a serious complication, leading to functional deficits, prolonged hospitalization, increased healthcare costs, and delays in adjuvant therapy [4-6]. While technical and perioperative factors are typically scrutinized, the role of underlying hypercoagulability is often underrecognized [7-9].

Factor V Leiden (FVL) is the most prevalent inherited thrombophilia, particularly among Caucasian populations, with heterozygous carriage in approximately 3–8% [10]. The Arg506Gln mutation in the *F5* gene renders factor V resistant to inactivation by activated protein C, impairing physiologic anticoagulant mechanisms and increasing thrombotic risk, by 3- to 8-fold in heterozygotes and up to 80-fold in homozygotes [11-12]. Despite its frequency, the impact of FVL on free flap outcomes in head and neck microsurgery remains poorly characterized. Existing literature is limited to small case series or individual reports, often involving patients with a prior diagnosis of thrombophilia [15-16]. The absence of standardized perioperative anticoagulation protocols for these patients has contributed to significant variability in clinical management [15-17].

We present a case of early free flap failure due to both arterial and venous thromboses in a patient ultimately found to have previously undiagnosed heterozygous FVL. The patient underwent successful contralateral fibula free flap reconstruction using a modified anticoagulation protocol. This case highlights the importance of considering occult thrombophilia in unexplained flap failure and demonstrates how adaptive perioperative strategies can mitigate risk in subsequent reconstruction.

CASE REPORT

A 71-year-old male with a history of hypertension, hyperlipidemia, cardiac arrhythmia, and prior laryngeal carcinoma was referred to the UAB Oral and Maxillofacial Surgery department in July 2024 after presenting to his general dentist with complaints of loose teeth. His oncologic history included a cordectomy, suspension laryngectomy, and adjuvant radiotherapy (66 Gy) administered between 2019 and 2021. The radiation field was confined to the larynx and did not include nodal mapping or elective neck irradiation. He had no personal or family history of venous thromboembolism (VTE).

Biopsy of the mandibular gingiva and computed tomography (CT) imaging were consistent with cT4aN2bM0 squamous cell carcinoma of the anterior mandible. Following multidisciplinary tumor board review, the patient elected to proceed with composite resection and immediate reconstruction.

A left neck dissection (levels Ia, Ib, IIa, IIb, III, IV, and V) was performed followed by segmental mandibulectomy. The defect was reconstructed with a three-segment fibula free flap incorporating an 8×12 cm skin paddle. No boluses of low molecular weight heparin (LMWH) or unfractionated heparin (UFH) were given prior to the initial microvascular anastomosis attempt. Papaverine was applied to the recipient vessels to promote vasodilation. During microvascular anastomosis, both arterial and venous connections thrombosed repeatedly. The initial attempt to anastomose the flap's vena comitans to the left common facial vein and the flap's artery to the left facial artery resulted in rapid thrombosis. A subsequent arterial anastomosis to the left lingual artery also thrombosed shortly after creation. Multiple re-anastomoses were required before adequate flow was established in the left lingual artery. A bolus of intravenous UFH was administered after initial thrombus formation was observed, and the flap was flushed directly with heparinized saline after each failed anastomosis. No streptokinase was used. Satisfactory perfusion was confirmed intraoperatively by Doppler signal and capillary refill. Postoperatively, fluid balance and hydration status were closely monitored, and normothermia was maintained. Enhanced Recovery After Surgery (ERAS) protocol was followed. Weight-based LMWH (0.4-0.5 mg/kg twice daily) was given but acetylsalicylic acid (ASA) was not due to early flap failure.

On postoperative day one, flap monitoring revealed loss of Doppler signal and flap pallor. Emergent re-exploration demonstrated both arterial and venous thrombosis at the anastomosis sites. Despite systemic heparinization and multiple attempts at thrombectomy, catheterization, and revision anastomosis, the flap could not be salvaged and was abandoned. The neck wound was closed, and alternative reconstructive options were discussed

with the patient and his family.

Given the rapid and unexplained thrombotic failure, hematology was consulted. Initial laboratory testing revealed abnormal activated protein C resistance, raising strong suspicion for an underlying thrombophilia. Due to the functional and oncologic implications of delaying reconstruction, the full hematologic workup was not yet complete at the time of the second fibula free flap. The patient was therefore managed under the working assumption that he likely possessed coagulopathy. Genetic testing later confirmed a heterozygous FVL mutation.

Ten days after the initial reconstruction attempt, a second free flap procedure was performed using the contralateral fibula, as the size of the defect was deemed incompatible with functional recovery and timely initiation of adjuvant radiation therapy. A bolus of 5,000 units of intravenous UFH was administered prior to the initial microvascular anastomosis attempt. The anastomosis utilized the right facial artery for simpler access despite increased morbidity associated with crossing the midline. This first anastomosis developed clotting and required revision. After thrombosis was observed, the flap was flushed directly with heparinized saline, and an additional 5,000 units of UFH was administered to achieve a supratherapeutic activated partial thromboplastin time (aPTT) of approximately 200 seconds. The second anastomosis attempt was then successfully completed. Postoperatively, intravenous UFH infusion was initiated and continued for three days in the intensive care unit (ICU), with dosing adjusted to maintain an aPTT target of 100 seconds. The ERAS protocol was followed, and hourly flap monitoring was maintained throughout the hospital stay. On post-operative day four, the patient was transitioned to weight-based LMWH dosing and subsequently to fixed dose LMWH (30 mg twice daily) and ASA (325 mg daily via PEG tube) for VTE prophylaxis.

Representative intraoperative and postoperative photographs are provided in Figures 1–4, illustrating the explanted flap, the revised recipient site, revision flap inset, and final closure. The second flap remained viable throughout the postoperative period, with strong Doppler signals and no clinical signs of compromise. The patient tolerated the anticoagulation regimen well and was discharged home on postoperative day twelve without complications.

The patient passed away during the follow-up period from causes unrelated to the surgery or its immediate complications. As a result, a direct patient perspective could not be obtained. The authors acknowledge the importance of including patient-reported experiences in case reporting and regret this limitation.

DISCUSSION

This case represents a rare occurrence of intraoperative and postoperative arterial and venous thromboses during fibula free flap reconstruction of the mandible in a patient with previously undiagnosed heterozygous FVL. While FVL is primarily associated with venous thrombotic events, the manifestation of concomitant arterial thrombosis in microsurgical reconstruction is uncommon and poses significant diagnostic and management challenges [16, 18-21]. Most large studies have not shown a significantly increased risk of arterial thrombosis in FVL-positive patients [10, 24-26], although mixed reports exist in the literature [16, 29], making this dual presentation particularly noteworthy and underscoring the need for heightened clinical suspicion and adaptive perioperative planning.

FVL is a well-established risk factor for perioperative venous thromboembolism and has been linked to increased rates of free flap thrombosis and failure, with poor salvage outcomes frequently reported despite prompt intervention [16, 18, 24-28]. Faber et al. (2011) conducted a retrospective review of microvascular reconstructions complicated by unexplained thrombosis and found that flap failure was often the first sign of an underlying thrombophilia such as FVL, with salvage attempts proving unsuccessful [29]. Based on these findings, they advocated for targeted thrombophilia screening in patients with unexplained or recurrent thrombosis and proposed an aggressive, individualized anticoagulation protocol: preoperative LMWH, intraoperative continuous intravenous UFH with aPTT monitoring, and postoperative continuation of anticoagulation until discharge. Case reports such as that by Lugo et al. (2017) provide additional insights, demonstrating that successful free tissue transfer can be achieved in patients with inherited thrombophilia through coordinated multidisciplinary planning and a tailored anticoagulation regimen [30]. In their case, a patient with a strong personal and family history of VTE who was heterozygous for FVL underwent osteocutaneous scapular free flap reconstruction

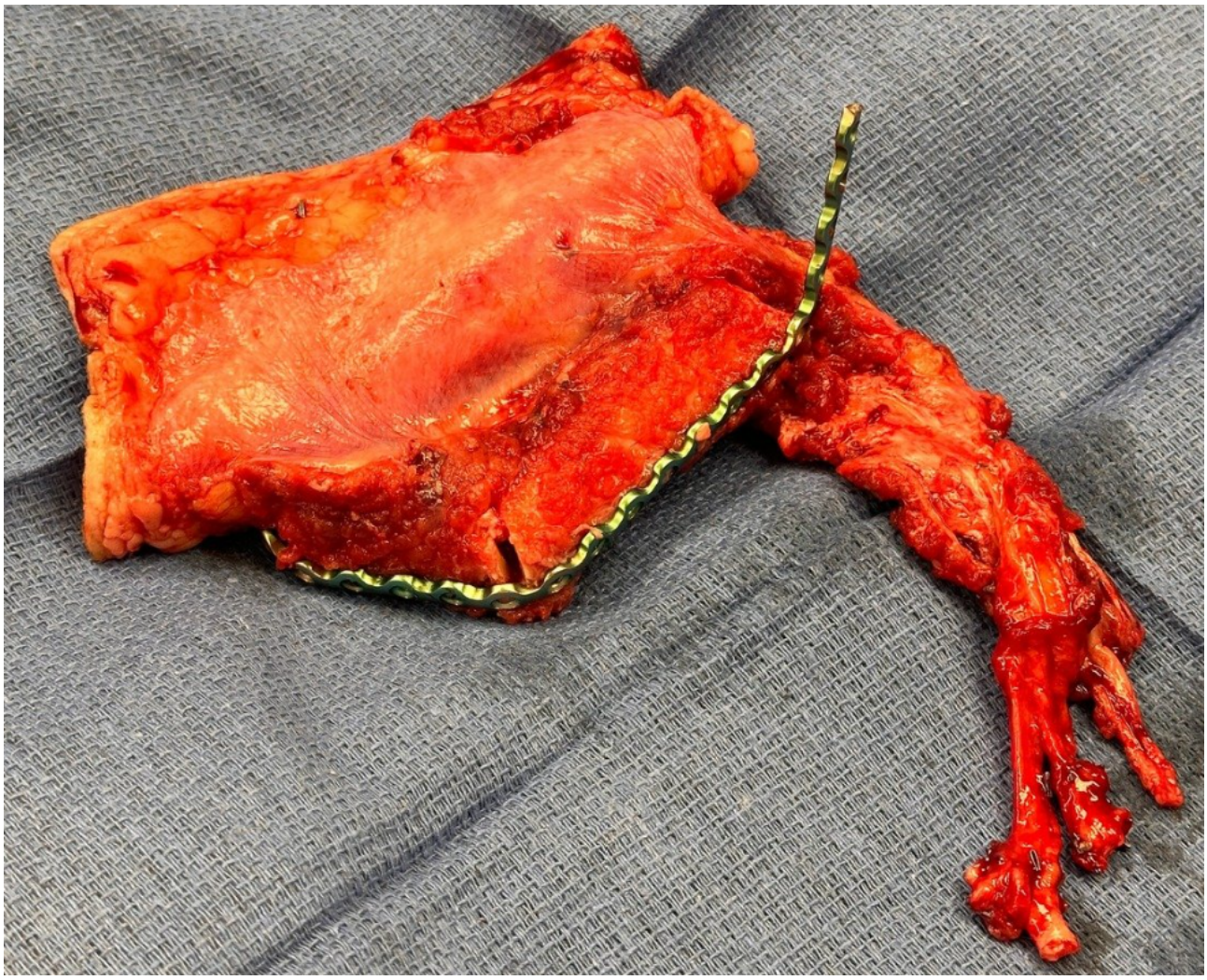

FIGURE 1. Revision osteocutaneous fibula free flap specimen prior to inset. Intraoperative photograph demonstrating the revision three-segment osteocutaneous fibula free flap. The image shows the skin paddle, vascular pedicle, and segment of fibula bone with fixation hardware.

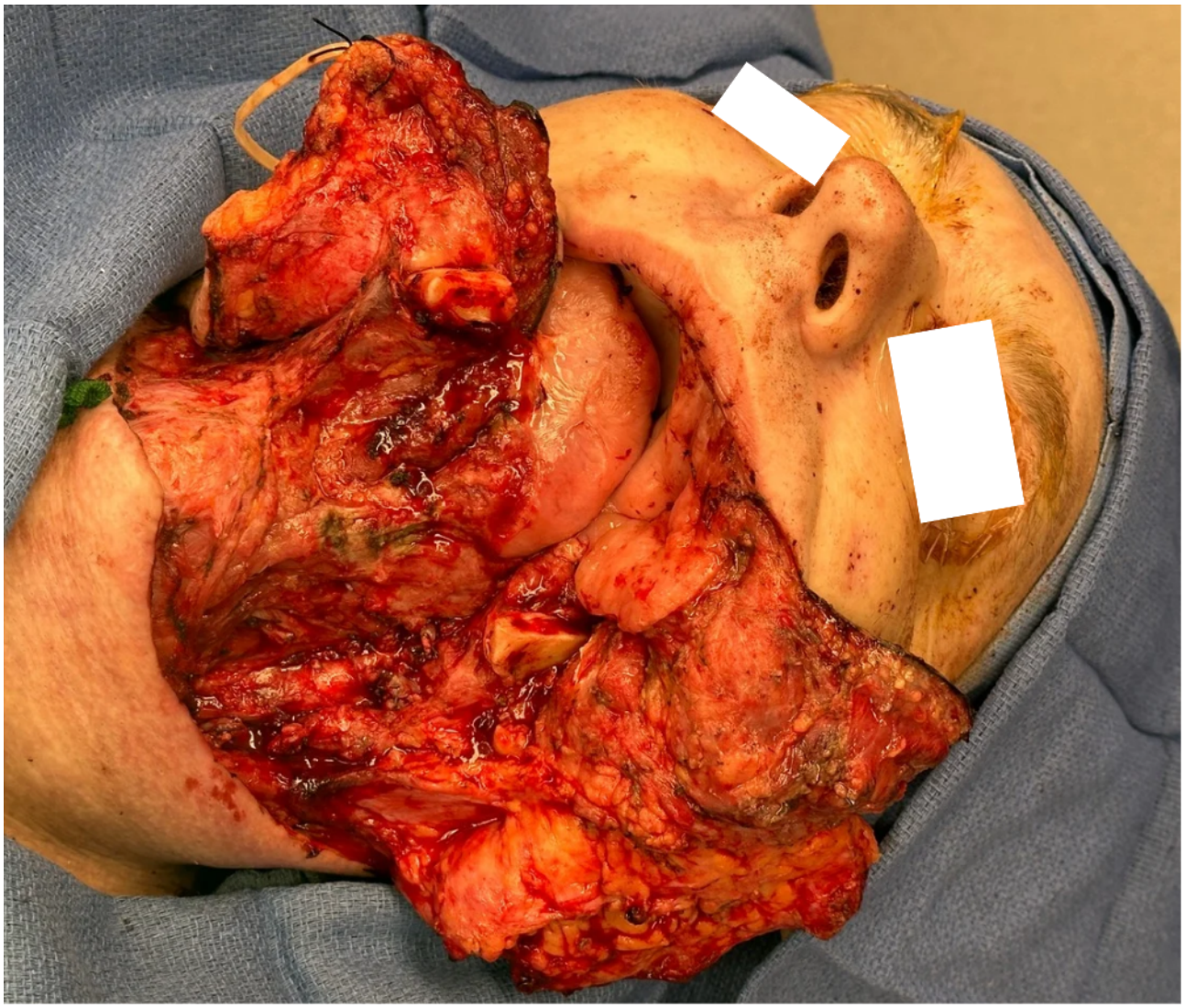

FIGURE 2. Recipient site following removal of primary osteocutaneous fibula free flap. Intraoperative view of the recipient site after explantation of the primary osteocutaneous fibula free flap. Extensive soft tissue and bony defect of the lower face and mandible is visible.

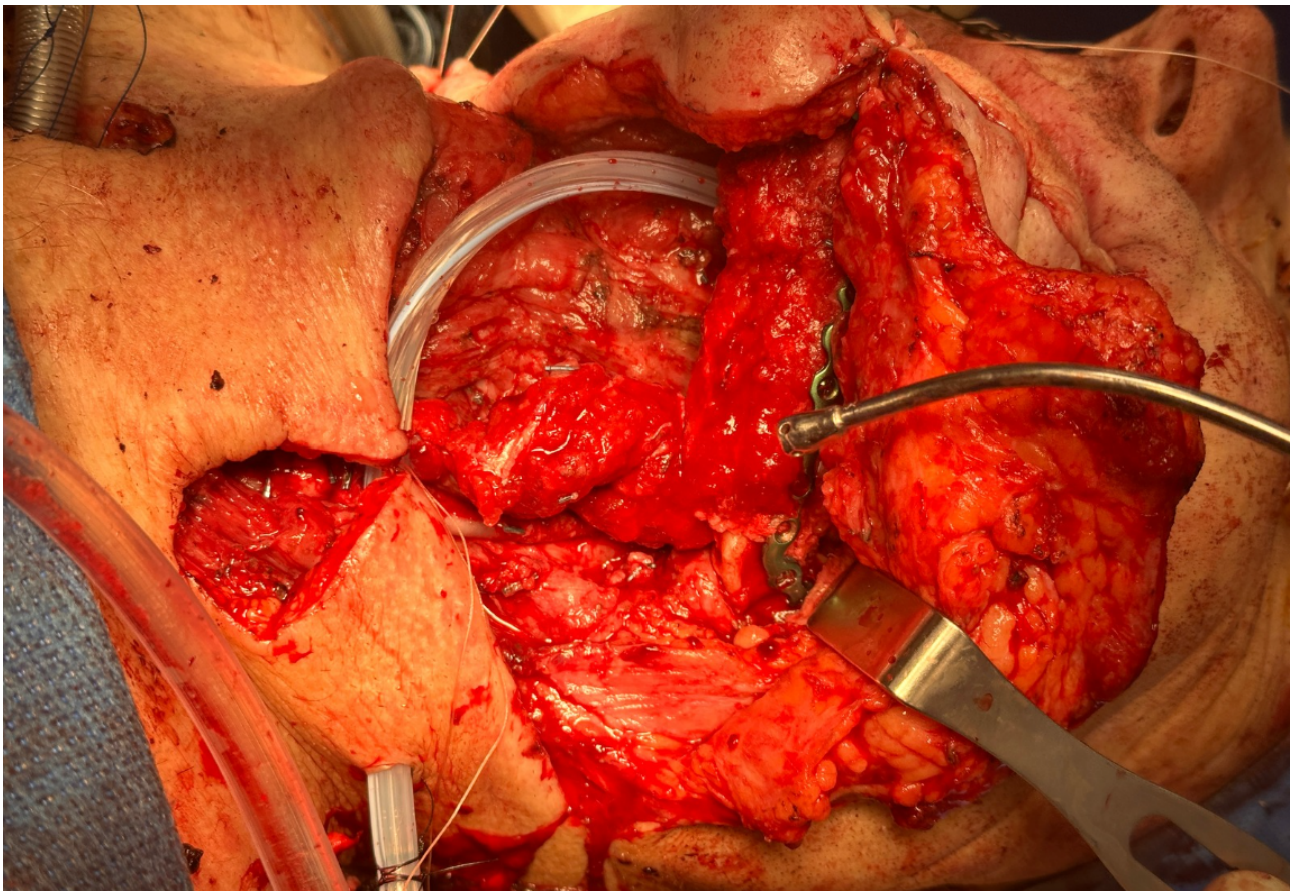

FIGURE 3. Inset of revision osteocutaneous fibula free flap. Intraoperative photograph showing the revision osteocutaneous fibula free flap after inset into the defect site. The fibular bone segment is secured in position with fixation hardware, and the skin paddle and soft tissue components are oriented for reconstruction of the composite defect.

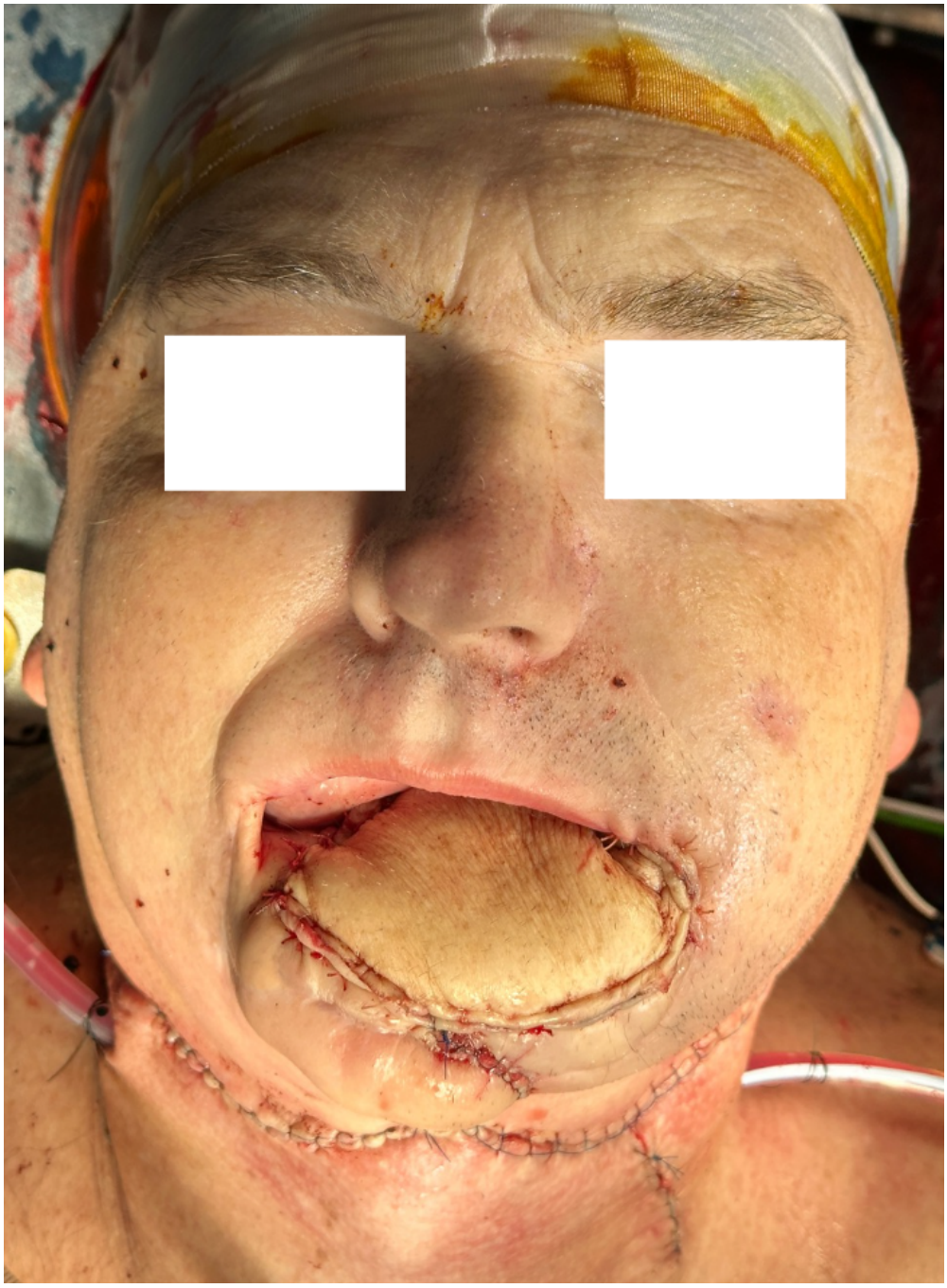

FIGURE 4. Immediate postoperative result following revision osteocutaneous fibula free flap reconstruction. Clinical photograph demonstrating the patient immediately after skin closure. The flap skin paddle is clearly visible inset into the facial defect, with the incision lines closed primarily.

without complications, utilizing intraoperative heparin followed by postoperative aspirin and LMWH. The experiences of Faber et al. and Lugo et al. suggest that individualized perioperative care is essential, and that a range of anticoagulation strategies can be safely and effectively employed in patients with FVL.

In a retrospective study, Wang et al. (2017) evaluated 41 hypercoagulable patients undergoing free flap reconstruction, including those with FVL and several other thrombophilias, and observed notably high rates of flap thrombosis (20.7%) and flap loss (15.5%) [20]. Many of these patients had a history of thrombotic events before the age of 50, an important clinical clue that should raise suspicion for an underlying thrombophilia and prompt further evaluation. Importantly, in this cohort, no postoperative thrombosed flaps were successfully salvaged, despite aggressive management, and most thromboses occurred in the delayed postoperative period. These findings suggest that while free tissue transfer can be feasible in patients with thrombophilia, the risk of thrombotic complications and failed salvage is significantly increased. Clinicians should be vigilant in identifying patients at risk, seek multidisciplinary perioperative planning, and ensure close postoperative monitoring.

Therapeutic anticoagulation may not be a simple or definitive solution for free flap patients with thrombophilia. Nguyen et al. (2019) retrospectively analyzed 28 free flaps in 24 patients with diagnosed thrombophilias [31]. Although they achieved 100% flap survival, 43% of patients experienced complications, including flap thrombosis, hematoma, pulmonary embolism, or deep vein thrombosis. They found that therapeutic heparin infusion was associated with an increased risk of hematoma. This observation is supported by Dawoud et al. (2021), whose meta-analysis of over 3,500 free flaps found that therapeutic-dose anticoagulation did not significantly reduce the rates of thrombosis or flap loss, but did significantly increase the risk of hematoma and bleeding complications [32].

The exact mechanism underlying the increased risk of hematoma and bleeding complications with therapeutic heparin anticoagulation in these patients remains unclear, though several factors may play a role. These patients have a persistent prothrombotic tendency that can overwhelm the effects of standard heparin dosing, particularly if anticoagulation is subtherapeutic or interrupted [17, 31-32]. Surgical trauma further amplifies this risk by promoting endothelial injury and hypofibrinolysis [17]. While heparin is known to enhance antithrombin III activity to inhibit thrombin and factor Xa, it does not effectively suppress platelet activation or aggregation, processes that are particularly important in microvascular thrombosis [17]. Platelet-driven clot formation can occur independently of the pathways targeted by heparin, meaning that microthrombi at the anastomosis site may still develop even in the presence of systemic anticoagulation. Moreover, heparin has been shown in some contexts to paradoxically activate platelets, particularly at certain dosages or in susceptible individuals, further promoting platelet-rich thrombus formation [17]. Thus, therapeutic heparinization may not fully protect against microvascular thrombosis and may contribute to persistent hematologic complications in patients with FVL undergoing free tissue transfer.

It can be argued that routine preoperative thrombophilia screening in head and neck microvascular surgery may enable more individualized anticoagulation and potentially reduce the risk of perioperative thrombotic complications and flap loss. Such screening may also help guide long-term risk counseling for patients and their families. However, we support current guidelines from the American Society of Hematology and the Enhanced Recovery After Surgery Society, which recommend selective, risk-based testing [31-33]. Our experience, including the presented case, suggests that current guideline recommendations for selective thrombophilia screening are reasonable when paired with a thorough clinical history. Careful assessment often suffices to identify patients at increased risk and guide management. Still, we acknowledge that even detailed histories may fail to uncover occult hypercoagulable states, leaving a subset of at-risk individuals unidentified. In this case, targeted evaluation and close collaboration with hematology enabled successful outcomes without unnecessary testing or overtreatment, further supporting the clinical validity of a selective approach. However, the limitations of history-based risk stratification highlight the need for further research and development of improved screening tools to better identify and manage high-risk patients in this population.

It is important to note that while previous radiotherapy can increase technical complexity of microvascular surgery due to vessel fibrosis or

friability [34-37], there is no strong evidence that it directly predisposes to flap thrombosis [38-40]. As such, prior radiation for laryngeal cancer was unlikely to have significantly contributed to flap failure in this patient. The decision to use the chosen recipient vessels was based on accessibility and vessel quality, rather than any limitation imposed by prior radiotherapy. ERAS principles were followed as closely as the clinical context permitted, making it unlikely that deviation from standard perioperative protocol contributed to the flap failure [41-42].

Early consideration of thrombophilia should be part of the diagnostic workup for unexplained flap thrombosis, as individualized, multidisciplinary management can optimize outcomes even after initial failure. Based on our experience and current literature, we believe that in cases where an initial free flap fails without an identifiable technical or systemic cause, a thrombophilia workup should be strongly considered. If testing cannot be completed in time, but clinical suspicion of an occult hypercoagulable state remains high, we recommend bolusing with 5,000 units of intravenous UFH prior to revision microvascular surgery. If intraoperative clotting is encountered, additional bolusing of UFH should be considered to achieve a supratherapeutic aPTT. This should be followed by postoperative maintenance of a therapeutic aPTT target of 100 seconds or more in the intensive care setting. This strategy may provide a practical and adaptable pathway for optimizing outcomes in patients with suspected but unconfirmed thrombophilia.

The generalizability of this case is limited by its single-patient nature, and most available literature consists of retrospective series and case reports, both prone to selection and publication bias. Clinical investigation for thrombophilia in microvascular failure remains uncommon, likely resulting in underdiagnosis and hindering the development of universal, evidence-based guidelines. To advance the field, prospective studies are needed to clarify optimal screening, perioperative management, and standards of care for these complex patients, but this is difficult given the low prevalence of these coagulopathies.

CONCLUSION

This case highlights the challenges of microvascular reconstruction in patients with unrecognized hypercoagulable disorders. Early flap failure due to occult heterozygous factor V Leiden was successfully managed through targeted diagnosis and tailored anticoagulation, resulting in a favorable outcome. In the continued absence of standardized protocols for thrombophilia management in head and neck microsurgery, our experience underscores the importance of individualized risk assessment, early involvement of hematology, and adaptable perioperative strategies. Based on our clinical experience, we recommend that in cases of unexplained flap thrombosis with high suspicion of an underlying coagulopathy, especially when thrombophilia workup cannot be completed expeditiously, surgeons consider a proactive anticoagulation strategy. This includes administering intravenous UFH prior to microvascular anastomosis. If clotting is observed intraoperatively, additional UFH boluses may be used with a minimum target aPTT of 100 seconds maintained postoperatively. Careful evaluation of unexplained flap thrombosis for potential underlying coagulopathies may contribute to improved reconstructive outcomes and should be integrated into the management of similarly complex cases.

Statements and Declarations

Funding
No funding, grants, or other support was received for conducting this study or preparing this manuscript.

Competing Interests
The authors have no relevant financial or non-financial interests to disclose.
No funding, grants, or other support was received for conducting this study or preparing this manuscript.
All authors certify that they have no affiliations with or involvement in any organization or entity with any financial or non-financial interest in the subject matter or materials discussed in this manuscript.
The authors have no financial or proprietary interests in any material discussed in this article.

Author Contributions
Bryce Thornton, BS: Drafted the manuscript, performed literature review, data collection and figure preparation, and coordinated manuscript revisions.

Noah Rothman, BS: Assisted with data collection, literature review, and manuscript drafting and revision.

Kirav Patel, MD: Provided clinical expertise and reviewed the manuscript for important content.

Michael T. Kase, DMD: Contributed to patient care, clinical documentation, and critical revision of the manuscript.

Anthony B. Morlandt, DDS, MD: Served as the ablative surgeon, contributed to patient management and surgical details, and provided critical review and revisions of the manuscript.

Jay Ponto, DDS, MD: Supervised the project and provided mentorship, served as microvascular reconstructive surgeon, and critically revised the manuscript for final approval.

All authors read and approved the final manuscript.

Ethics Approval
The study was determined to be exempt from IRB review and does not require formal ethics approval.

Consent to Participate
Not applicable; the patient is deceased.

Consent to Publish
Not applicable; the patient is deceased.

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