Introduction
During the past decades a decreasing incidence of complications in cervicofacial abscess has been reported, as well as a decline in morbidity and mortality, thanks to the introduction of antibiotics and to an earlier and more detailed diagnosis by improved high resolution imaging techniques [1].

However, both the inevitable increase of antibiotic resistance and a higher number of immunosuppressed patients introduced new challenges in the management of these pathologies.

Risks in cervicofacial abscesses are related to the potential spread of the infectious process among neck spaces and to critical areas apart from the neck as well as involving the anterior mediastinal area, the orbit, the skull base and the endocranium, together with general septic complications that may occur [2-4].

The real incidence of cervicofacial abscesses cannot be easily assessed, [5]. The highest incidence in children is reported around 6; this is associated to immaturity of immune system and to hypertrophy of retropharyngeal lymph nodes that undergo spontaneous regression after 5 [5-8]. In adults, instead, the peak of incidence for infections affecting the deep neck spaces is between the fifth and the sixth decades [9].

Many of the bacterial pathogens involved in cervicofacial abscesses might be connected to acquired resistance to antibiotics which should normally be effective [10]. Awareness on this problem is of great importance especially when empirical antibiotic treatment must be planned, before culture studies or when culture results are not available as often occurs in clinical practice. Currently, the main problems related to acquired resistance are posed by Gram-positive cocci such as *Streptococcus spp.*, *Staphylococcus aureus*, *H. influenzae* and, to a limited extent, anaerobic bacteria [11].
β-hemolytic streptococcus still remains uniformly susceptible to penicillin and to other beta-lactam antibiotics while problems of acquired resistance to macrolides, lincosamides and tetracycline are reported [12].

Likewise, problems related to acquired resistance have been reported also for *S. pneumoniae*. Moreover, since the 80s, a spread of *S. pneumoniae* strains showing reduced susceptibility to penicillin mediated by target modifications (penicillin-binding proteins - PBP) has been reported worldwide.

The present study aims at investigating, through a retrospective analysis, parameters that may have an effect on the clinical course and consequently on the management of patients presenting with a neck abscess.

### Methodology

**Study design**

Medical records of 394 patients diagnosed with abscess and admitted to the Otorhinolaryngology Clinic at Sassari University between 2009 and 2017 were reviewed.

For each patient the following parameters were evaluated: age, gender, clinical picture at admission, infection site, microbiology, comorbidity, diagnosis of diabetes mellitus, immunodeficiency due to HIV, complications, medical treatment, antimicrobial therapy used, allergy to antibiotics, duration of hospital stay and recovery following surgical treatment, possible sequelae after surgery, blood parameters. Administered treatments were classified using a score ranging from 1 (= antimicrobial medical treatment alone) to 2 (= medical treatment + transoral drainage), and 3 (external/open drainage approach needed).

**Clinical target**

To define the site, the most recent classifications in the literature were taken into consideration for what concerns the spaces in the neck that might be filled by abscesses [13]. Therefore, abscesses were classified based on involvement of the following spaces: peritonsillar, submandibular and sublingual, parapharyngeal, masticatory, parotid, anterior visceral, retropharyngeal, carotidial and prevertebral.

Blood parameters analyzed were: number of white blood cells, percentage of neutrophils, percentage of lymphocytes, HGB, glycemia, creatininemia, ESR and C-reactive protein, serum Na+ and K+. The collected parameters were used to compute the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score [14]. Patient values were examined at hospital admission, 5 days after hospitalization, and at discharge. Statistical description and correlation were performed on JMP 7.0.1 (SAS Institute Inc.).

### Results

The total number of patients observed between 2009 and 2017 was 394 (269 male and 125 female patients), with an average of 44 hospitalizations per year. Among these, 11 (2.8%) were complicated by necrotizing fasciitis (NF). Mean age was 41 (±17) years, ranging from 9 to 87 years of age.

Descriptive statistics is shown in Table 1.

Based on anamnesis and objective findings, patients presented with the following signs and symptoms: pharyngodynia (reported 256 times), cervical swelling (76), dysphagia (246), odynofagia (147), hyperpyrexia (159) and reflex otalgia (49), trismus (43), dysphonia (29), and hypersalivation (5). Foreign body sensation was observed in 40 (10.1%) patients.

### Table 1

| Variables                      | N = 394 |
|-------------------------------|---------|
| Gender, n (%)                 |         |
| Male                          | 269 (68%) |
| Female                        | 125 (32%) |
| Age                           |         |
| Mean (SD)                     | 41 (+/-17) |
| SITE, n (%)                   |         |
| Peritonsillar                 | 303 (76.9%) |
| Parapharyngeal                | 42 (10.6%) |
| Submandibular and sublingual  | 39 (9.9%) |
| Masticatory                   | 4 (1%) |
| Parotidal                     | 11 (2.8%) |
| Anterior visceral             | 15 (3.8%) |
| Retropharyngeal space         | 3 (0.8%) |
| Carotidial                    | 3 (0.8%) |
| Two or more sites             | 28 (7.1%) |
| Necrotizing fasciitis (NF)    | 11 (2.8%) |
| Signs and symptoms, n (%)     |         |
| Pharyngodynia                 | 256 (65%) |
| Cervical swelling             | 76 (19.3%) |
| Dysphagia                     | 246 (62.4%) |
| Odynophagia                   | 147 (37.3%) |
| Hyperpyrexia                  | 159 (40.3%) |
| Reflex otalgia                | 49 (12.4%) |
| Trismus                       | 43 (10.9%) |
| Dyspnea                       | 28 (7.1%) |
| Epiglottis edema              | 15 (3.8%) |
| Redness                       | 3 (0.8%) |
| Cervical numbness             | 3 (0.8%) |
| Stomatolalia                  | 10 (2.5%) |
| Dysphonia                     | 29 (6.8%) |
| Hypersalivation               | 5 (1.3%) |
| Foreign body sensation        | 3 (0.8%) |
| Other complaints (pain, tenderness, headache, other) | 40 (10.1%) |
| Comorbidities, n (%)          |         |
| Diabetes                      | 25 (6.3%) |
| Other types of immunodeficiency | 11 (2.8%) |
(159), reflex otalgia (49), trismus (43), dyspnea (28), epiglottis (15), redness (3), cervical numbness (3), stomatolalia (10), dysphonia (29), hypersalivation (5), foreign body sensation (3) and other complaints including pain, tenderness and headache (40).

The most recurrent site involved was the peritonsillar (303 cases), followed by the parapharyngeal (42), submandibular and sublingual sites (39), masticatory (4), parotideal (11), anterior visceral (15), retropharyngeal (3), carotideal (3) and prevertebral (0); a total of 28 (7.1%) patients presented visceral (15), retropharyngeal (3), carotideal (3) and peritoneal (0); a total of 28 (7.1%) patients presented with symptoms involving two or more than two sites.

For each patient a sample was collected for culture examination and antibiogram.

Among comorbidities, 25 patients with diabetes were reported and 11 presenting with other types of immunodeficiency.

Eleven cases of NF and two cases of jugular vein thrombosis were reported, associated with other complications such as respiratory failure, pneumothorax, pleural effusion, sepsis, hemorrhage.

Patients underwent medical (antibiotic therapy, corticosteroids) and surgical treatment (transcervical or transoral drainage). Forty-nine patients underwent medical therapy alone, while medical therapy plus transoral drainage was performed on 294 patients and medical treatment plus transcervical drainage in 51 cases.

Microbiological exam of the drained material collected through swabs was performed in all cases requiring an external approach (51), and in 53 out of 294 patients treated with transoral drainage. No clear differences where observed among the microbiological findings in patient drained transorally, patients drained through a cervicotomy or patients evolving in NF.

Thirty-one cases (30%) had more than a pathogen isolated from the swab, in 20 cases (19%), all already under antibiotic treatment, the swab was negative. The most frequently isolated genera were: Streptococcus spp (34 cases), followed by Staphylococcus spp (27). In 53 cases (51%) a single pathogen was isolated. The most frequently isolated single pathogen was Streptococcus Viridans (20 cases), followed by Streptococcus Anginosus (18 cases).

Most frequently used antibiotics were penicillin (250 patients; 64%) and cephalosporins (113 patients; 29 %), followed by lycosamids, macrolides, glycopeptides and nitroimidazole compounds.

An average of 6 days of hospitalization has been recorded, ranging from a minimum of 1 to a maximum of 100 days.

Blood parameters mean values: white blood cells 15.55×10³/mL (±6.22) (normal values v.n 4.80 -10.80), neutrophils 78.98 (±12.35) (v.n 40 – 74); lymphocytes 12.40 (±8.47) (v.n. 19 – 48); hemoglobin 13.97 (±6.01) (v.n. 13 – 17); creatininemia 0.8 mg/dL (±0.2) (v.n. 0.64 – 1.04); ESR 47 (±25) mm/h (v.n. 0 – 20); C-reactive protein 8.57 (±8) mg/dL (v.n. 0 – 8); glucose 114 (±48) mg/dL (v.n. 60 – 110 mg/dL).

For what concerns the latter, fifty-seven patients were reported at time of admission as having glucose values over 130 mg/dL (hyperglycemic patients), 269 were reported as non-hyperglycemic. Blood parameters mean values were: white blood cells 15.55×10³/mL (±6.22) (normal values v.n 4.80 -10.80); neutrophils 78.98 (±12.35) (v.n. 40 – 74); lymphocytes 12.40 (±8.47) (v.n. 19 – 48); hemoglobin 13.97 (±6.01) (v.n. 13 – 17); creatininemia 0.8 mg/dL (±0.2) (v.n. 0.64 – 1.04); ESR 47 (±25) mm/h (v.n. 0 – 20); C-reactive protein 8.57 (±8) mg/dL (v.n. 0 – 8); glucose 114 (±48) mg/dL (v.n. 60 – 110 mg/dL).

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| Table. 1 (continued) Analytical description of clinical cases. |
|---------------------------------------------------------------|
| **Variables** | N = 394 |
| **Treatment** | |
| Medical treatment alone (antibiotic + corticosteroids) | 49 (12.4 %) |
| Medical treatment + transoral drainage | 294 (74.6 %) |
| - Microbiological exam performed | 53/294 (18%) |
| Medical t. + transcervical drainage | 51 (12.9 %) |
| - Microbiological exam performed | 51/51 (100%) |
| **Pathogen isolated in 104 swabs, n (%)** | |
| More than a pathogen | 31 (29.8 %) |
| Single pathogen | 53 (13.5 %) |
| Swab negative (all already under antibiotic treatment) | 20 (5 %) |
| **Antibiotic treatment** | |
| Penicillins | 250 (63.4%) |
| Cephalosporins | 113 (28.7%) |
| other | 13 (3.3%) |
| **Blood parameters mean values, n (SD)** | |
| White blood cells (v.n. 4.80-10.80) | 15.55×10³/mL (±6.22) |
| Neutrophils (v.n. 40 – 74) | 78.98 (±12.35) |
| Lymphocytes (v.n. 19 – 48) | 12.40 (±8.47) |
| Hemoglobin (v.n. 13 – 17) | 13.97 (±6.01) |
| Creatininemia (v.n.0.64 – 1.04) | 0.8 mg/dL (±0.2) |
| ESR (v.n. 0 – 20) | 47 (±25) mm/h |
| C-reactive protein (v.n. 0 – 8) | 8.57 (±8) mg/dL |
| Glucose (v.n. 60 – 110 mg/dL) | 114 (±48) mg/dL |

Blood parameters mean values were: white blood cells 15.55×10³/mL (±6.22) (normal values v.n. 4.80 -10.80); neutrophils 78.98 (±12.35) (v.n. 40 – 74); lymphocytes 12.40 (±8.47) (v.n. 19 – 48); hemoglobin 13.97 (±6.01) (v.n. 13 – 17); creatininemia 0.8 mg/dL (±0.2) (v.n. 0.64 – 1.04); ESR 47 (±25) mm/h (v.n. 0 – 20); C-reactive protein 8.57 (±8) mg/dL (v.n. 0 – 8); glucose 114 (±48) mg/dL (v.n. 60 – 110 mg/dL).
Glucose: values < 180 = 0 ; ≥ 180 = + 1. The mean LRINEC value was 0.77 (±1.3).

At statistical analysis, higher C-reactive protein, glycemia and creatininemia were all associated to longer hospital stay and to the need for an external drainage of the abscess. Higher LRINEC score is associated to higher risk of NF.

Out of a total of 394 patients only one patient died, who belonged to the group of patients affected by NF.

**Discussion**

Comparing data resulting from this study to literature, a different demographic composition emerged in regards to other studies: in the present study the male population is slightly larger (68%) [15]. Age ranges between 9 and 87 years with an average age of 41 years.

As previously highlighted in the literature, the most frequently affected site was the peritonsillar (76,9%), followed by the parapharyngeal space (10,6%) [16].

The clinical picture is homogeneous to other studies, being pharyngodynia, odynophagia, dysphagia the most important symptoms.

The study aimed also at understanding if there is a correlation among the different parameters under analysis and if they are implicated in clinical outcome. Using different statistical tests (t test, linear fitting) we evaluated which clinical and patient’s parameters mostly influenced the clinical outcome at the same time allowing a prediction. Three parameters have been considered as clinical outcome indicators: hospitalization duration, need of external surgical treatment and the most fearsome development, being represented by NF.

Prior to admission, inadequate antibiotic therapies are usually prescribed by General Practitioners to the majority of patients. Narrow-spectrum antibiotics, in sub-therapeutic doses, given at first complaint expose patients to a higher risk of developing antibiotic resistance and to the evolution in abscesses.

Similarly to the findings of Kauffmann and Cordesmeyer, a significant proportion of patients displayed hyperglycemia at admission and in these cases the hospitalization time has been significantly longer [14-18].

Hyperglycemia, as demonstrated by other studies, leading to an immune system dysfunction, tends to prolong duration of hospital stay, especially in diabetes mellitus patients. Specifically, some studies identified a lack of complement component C4 and this reduction might be associated to a dysfunction of polymorphonuclear leukocytes and to a reduced cytokines responsiveness. In people affected by diabetes mellitus, monocytes show a reduced secretion of interleukin-1 (IL-1) and IL-6, induced by lipopolysaccharides. It seems that a low production of certain interleukins is caused by an intrinsic defect of immune cells in these subjects. Other studies reported that increase of glycation might inhibit IL-10 production by myeloid cells as well as production of interferon gamma (IFN-γ) and tumor necrosis factor (TNF-α) by T cells. Glycation reduces also the expression of major histocompatibility complex Class I (MHC) on myeloid cells surface, compromising cells immunity. In these patients polymorphonuclear leukocytes mobility is reduced as well as chemotaxis and phagocitary activity. The hyperglycemic environment also blocks the antimicrobial function, by inhibiting glucose 6-phosphate dehydrogenase (G6PD), increasing leukocytes apoptosis and reducing leukocytes diapedesis.

Therefore, immune dysfunction in hyperglycemic patients and inadequate antibiotic therapy have a role in determining respectively a higher predisposition to persisting infections and antibiotic resistance, alongside with longer hospital stay. In addition to this, it must be taken into account that medical therapy includes also corticosteroids, which, among the other effects, exert a hyperglycemic effect.

As far as the LRINEC score is concerned, a low average score was observed in all patients except patients diagnosed with NF who showed a higher score. Among these, the LRINEC score was < 6 in four patients, in five patients it was ≥ 6, while data regarding two patients were missing. The average hospital stay in NF patients was 46 days, while mean duration of stay in intensive care unit (ICU) was 10,25 days for the first group (LRINEC < 6) and 26,2 for the second one (LRINEC > 6).

Only one patient out of 349 passed away (0,2%). However, this case is included among patients presenting with NF, so among patients with NF there was a mortality rate of 9%.

This is an indication that NF is a fearsome complication that needs to be treated rapidly and effectively. In our series, subjects diagnosed with NF were all referred to our facility after having already shown this clinical development, therefore it was probably the consequence of a neck abscess inadequately treated as outpatients.

**Conclusion**

Among all parameters analyzed, the glycemia, creatininemia and C-Reactive protein correlated with...
the duration of hospital stay which is notoriously a fair indicator of difficult clinical management.

A correct antibiotic therapy at the beginning, both in terms of dosage and spectrum, together with an adequate glycemic control might reduce hospital stay. Also, early diagnosis and an adequate timely medical-surgical treatment are crucial to reduce complications. In particular, empirical antibiotic therapy during early stages, based on epidemiological data, and adjusted basing on microorganism isolation, is crucial.

The LRINEC score can be considered a useful parameter to identify at early stage patients at risk of developing NF. Nevertheless, clinical and intraoperative assessments are the only reliable diagnostic parameter for NF itself.

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