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Management of oral feeding after total laryngectomy around the world: a YO-IFOS international study

Running title: oral feeding after total laryngectomy

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ABSTRACT

Objectives: To analyze the perioperative management and the protocols and practices regarding the initiation of oral feeding after total laryngectomy (TL) around the world.

Methods: An online survey was distributed by the head and neck Study Group of the Young Otolaryngologists of the International Federation of Oto-rhino-laryngological Societies (YO-IFOS).

Results: Among the 332 responses received, 278 from 59 countries were analyzed. For a patient who underwent TL without pharyngectomy and without prior radiotherapy and with primary mucosal closure, 45.6% of respondents started oral hydration (water) and 45.1% started liquid diet between postoperative day 7 and day 10. Semi-solid feeds were initiated between days 10 and 14 for 44.9% of respondents and a free diet was allowed after day 15 for 60.8% of respondents. The timing of initiation of oral fluids and feeds was significantly delayed in cases of TL associated with pharyngectomy, after prior radiotherapy, and when a flap was used for the reconstruction of a mucosal defect ($p<0.001$). A greater proportion of respondents in Africa and Oceania allowed early oral feeding between days 1 and 6 as compared to the rest of the world ($p<0.001$).

Conclusion: Despite increasing evidence in support of early oral feeding following TL, the majority of respondents preferred to delay the initiation of oral feeding until at least 7 days after surgery, or later, in case of high-risk individuals. The overall advantages of early oral feeding and the selection of patients who can benefit from it remains to be evaluated in depth.

Level of evidence: N/A

Key-words: laryngectomy, early oral feeding, head and neck cancer, Enhanced recovery after surgery

INTRODUCTION

Definitive or salvage total laryngectomy (TL) remains an important management option in the therapeutic algorithm of advanced laryngeal and hypopharyngeal cancer, despite an increase in organ preservation protocols. Total laryngectomies and pharyngo-laryngectomies still have well defined indications, especially in the following cases: advanced tumors (T4a); significant alteration of laryngeal functions; medical contraindications to optimal radio-chemotherapy; or following failure or recurrence after an organ preservation protocol.¹ Total laryngectomy is associated with multiple risks of local postoperative complications², among which the most frequent and serious is the development of a pharyngo-cutaneous fistula (PCF) with an incidence ranging from 10% to 34%.³ The occurrence of this complication significantly increases morbidity and mortality due to its association with an increased risk of infection, the requirement for revision surgery, a longer hospital stay, delays in the initiation of adjuvant therapy, and the risk of death following carotid blowout.³ Numerous risk factors for the development of PCF have been suggested in the literature with a significant variability between studies. The most commonly accepted risk factors are a history of prior irradiation, advanced tumor stage requiring extensive surgery, hypopharyngeal tumors, and a postoperative hemoglobin level < 99g/L.⁴⁻¹⁰ For a long period, the postoperative initiation of oral feeds was considered to be one of the main factors favoring the development of PCF. Therefore, it has been common practice to delay oral feeding for 10 or more days postoperatively.^{11,12} However, the role of oral feeding and its contribution to the development of PCF has since been questioned and there is a trend in the literature to encourage earlier initiation of oral feeding.¹³⁻¹⁵ This could have several advantages, including an improvement in the patient's quality of life, a reduction in the postoperative care required, and a shortened duration of hospital stay, all ultimately reducing management costs.¹⁶

The objectives of this international study were to investigate the protocols of initiation of oral feeding applied in different centers around the world, to analyze the differences in management between the different regions of the world, and to analyze the factors influencing the delay of initiation of oral feeding after total laryngectomy.

METHODS

Survey Development

The survey was developed via an iterative method by the head and neck Study Group of the Young Otolaryngologists of the International Federation of Oto-rhino-laryngological Societies (YO-IFOS), which includes head and neck experts from all continents. The questions were carefully chosen to explore the perioperative management of TL patients, particularly with regards to oral intake in different institutions around the world. The questionnaire was prepared with Survey Monkey (San Mateo, California, USA). The preliminary version of the questionnaire was sent to a committee comprising certified otolaryngologists from 5 continents and 14 countries (Argentina, Belgium, Brazil, Canada, Columbia, Italy, France, Lebanon, New Zealand, Singapore, Spain, South Africa, Thailand, and USA). The survey was then revised and completed based on their comments. The final version of the survey included 29 questions divided into 7 sections: general information, patient nutritional status assessment, technical considerations (type of mucosal sutures and methods followed to ensure the absence of pharyngocutaneous fistula before allowing oral intakes postoperative), and the management of oral intake in 4 scenarios:

- patients who underwent total laryngectomy without pharyngectomy and without prior radiotherapy and with primary mucosal closure
- patients who underwent a salvage laryngectomy after prior radiotherapy, without pharyngectomy and with primary mucosal closure
- patients who underwent total laryngectomy associated with pharyngectomy (total laryngopharyngectomy) for a tumor involving the hypopharynx, and without prior radiotherapy, with the concurrent use of a pedicled or free flap for the reconstruction of a mucosal defect of the pharynx

- patients who underwent salvage total laryngectomy associated with pharyngectomy (total laryngopharyngectomy) for a tumor involving the hypopharynx, after prior radiotherapy with the use a pedicled or free flap for the reconstruction of a mucosal defect of the pharynx

The Institutional Review Board of Aix-Marseille University (Marseille, France) approved the protocol (N° 2021-04-08-03).

Survey Spread

A link to the survey was emailed 4 times (this included an initial email followed by 3 reminders) to members of YO-IFOS and IFOS from February to April 2021. Each participant could complete the survey only once. The survey was also sent to the members of the following societies: African Head and Neck society (AfHNS), Asian Society of Head and Neck Oncology (ASHNO), Thai Society for Head Neck Oncology (TSHNO), French Society for Head Neck Oncology (SFCCF), Australian, Brazilian, Canadian, New Zealand Head and Neck Societies and Société internationale Francophone d'ORL (SIFORL).

Response Collection and Statistical Analysis

Responses were collected anonymously, and incomplete responses were excluded from the analysis. The country, city and the name of institution of every respondent were identified. Furthermore, only one response per institution was used for the statistical analysis. The responses were analyzed by geographic region, using the following categorization: Europe (EU), North America (N-AM), South and Central America (S-AM), Asia (AS), Oceania (OC),

and Africa (AF). Because the participants in North Africa countries are closely associated to the Middle Eastern ENT societies, their data was combined with that of the Middle East participants (ME/N-AF).

The categorical variables were described by their number and percentage. They were compared by the Chi-square test, by the Fisher test or by the Chi-square test with p-value simulation, depending on the application conditions. By default, this simulation was performed on 2000 random selections. The tests were performed in a two-sided situation and were considered statistically significant for $p \leq 0.05$. Statistical analysis was performed with RStudio Desktop 1.4.1106 software.

RESULTS

General information and geographical distribution

Although it was impossible to identify the exact number of surgeons who received the invitation to answer the questionnaire, due to the use of the diffusion method, we estimate that 4000 ENT specialists were offered the opportunity to participate in the study. Following the 3-month diffusion period, a total of 332 responses were obtained. Of these, 4 responses were excluded due to a lack of significant and important data (ranging from 65 to 96%). Furthermore, only one response per center was selected because of available data on each participant's country, city and institution of practice. This selection led us to exclude an additional 50 responses, resulting in a total of 278 analyzable responses from 59 countries (**fig 1**). Of all the surgeons who responded to the questionnaire, 146 (52.9%) practiced in university-affiliated hospitals, 63 (22.8%) practiced in cancer centers, 33 (12%) in community hospitals, and 17 (6.2%) in private institutions. Seventeen surgeons (6.2%) practiced in unspecified or other types of institutions, or provided more than 3 different answers, making it impossible to precisely define the type of practice in these responses (**fig 2**). Ninety-six (34.5%) centers reported performing fewer than 10 TL per year, 87 (31.3%) between 10 and 19 procedures per year, and 95 (34.2%) more than 20 procedures each year. A lower rate of centers from North America and Europe performed fewer than 10 TL per year as compared to centers in other continents ($p = 0.06$) (**table 1**). One hundred and fifteen (41.5%) participants reported performing less than 25% of salvage TL after radio(chemo)therapy, 102 (36.8%) between 25 and 50%, and 60 (21.7%) more than 50%, with significant differences according to geographical areas ($p < 0.001$) (**table 1**).

Organization of patient management

With regards to the preoperative assessment of patients' nutritional status, the body mass index was used by 57.6% of the respondents, albumin and pre-albumin measurement by 54.7%, percentage weight loss by 50.7%, and nutritional assessment questionnaires by 35.3%. Twelve point six percent of the respondents declared that they did not assess the nutritional status of patients before surgery. One hundred and fifty-four (55.4%) of the respondents reported that dieticians or nutritionists were involved in the multidisciplinary team to assist with the nutritional management of all their patients, 95 (34.2%) only in cases of proven malnutrition, and 29 (10.4%) never, with significant differences according to geographical areas (**table 2**). Regarding the use of nutritional support during the postoperative period, most of the participants (96.8%) reported the use of a nasogastric tube. There were 191 (69%) who reported to using only this for nutritional support, 56 (20.2%) using either a nasogastric tube or gastrostomy, and 21 (7.6%) using either a nasogastric tube or intravenous infusion. Eight (2.9%) participants routinely made use of a gastrostomy, and 1 participant (0.4%) only used intravenous infusion. Concerning the methods used to ensure the absence of PCF before allowing oral intakes, 70.1% of respondents utilized a diagnostic test: blue methylene test for 121 respondents (43.5%) and Barium swallow test for 92 (33.5%), while 29.5% used clinical observation alone (0.4% of the participants did not answer this question). The tests were most often performed between 7 and 10 days after the surgery (for 48.8% of the respondents performing a blue methylene test and 52.2% Barium swallow test). Significant differences were found between geographical areas (**table 2**). The reported length of hospitalization after TL without postoperative complications was between 7 and 14 days for 52.3% of the respondents, between 14 and 21 days for 27.8%, within the first 7 days for 18.4%, and after 21 days for 1.4%. Significant differences were found between geographical areas (**table 2**). The estimated rate of PCF reported (overall estimation including all TL procedures) was less than 10% for 99 (35.9%)

respondents, between 10 and 25% for 127 (46%), between 25 and 50% for 42 (15.2%), and more than 50% for 8 (2.9%) (0.7% of the participants did not answer this question). Significant differences were found between geographical areas regarding a rate of PCF less than 10% (**table 2**). Our statistical analysis also showed that a greater proportion of respondents performing more than 25% of their TL as salvage surgery after radiotherapy reported a PCF rate greater than 10% compared to those performing less than 25% of salvage surgery (71.8% vs. 53.9% respectively, $p = 0.002$).

Characteristics	N-AM n = 23	S-AM n = 65	EU n = 98	AF n = 21	ME/N-AF n = 15	AS n = 46	OC n = 10	p-value
< 10 TL per year	6 (26.1%)	25 (38.5%)	25 (25.5%)	10 (47.6%)	5 (33.3%)	18 (39.1%)	7 (70%)	0.06
% post radiotherapy salvage TL > 25%	22 (95.7%)	36 (55.4%)	67 (68.4%)	1 (4.8%)	6 (40%)	23 (50%)	8 (80%)	<0.001

Table 1. General description according to geographical areas.

Characteristics	N-AM n = 23	S-AM n = 65	EU n = 98	AF n = 21	ME/N-AF n = 15	AS n = 46	OC n = 10	p-value
Collaboration with a dietician or a nutritionist	23 (100%)	60 (92.3%)	90 (91.8%)	14 (66.7%)	13 (86.7%)	39 (84.8%)	10 (100%)	0.015
Test used to ensure the absence of PCF	18 (78.3%)	46 (70.8%)	78 (79.6%)	7 (33.3%)	9 (60%)	28 (60.9%)	8 (80%)	<0.001
- Blue methylene test	5 (21.7%)	45 (69.2%)	51 (52%)	6 (28.6%)	5 (33.3%)	7 (15.2%)	2 (20%)	<0.001
- Barium swallow	14 (60.9%)	5 (7.7%)	37 (37.8%)	2 (9.5%)	5 (33.3%)	22 (47.8%)	7 (70%)	<0.001
Length of hospitalization ≤14 days	21 (91.3%)	62 (95.4%)	54 (55.1%)	12 (57.1%)	12 (80%)	27 (58.7%)	8 (80%)	<0.001
Rate of PC < 10%	2 (8.7%)	19 (29.2%)	28 (28.6%)	9 (42.9%)	10 (66.7%)	28 (60.9%)	3 (30%)	<0.001

Table 2. Organization of patient management depending on the geographical area

Time to postoperative initiation of oral feeds

For a patient who underwent TL without a pharyngectomy and without prior radiotherapy and with primary mucosal closure (case 1), 45.6% of respondents started oral hydration (water) between postoperative day 7 and day 10. The reintroduction of a liquid diet (e.g. juice, milk) was started between days 7 and 10 for 45.1% of respondents. Semisolid food (e.g. mixed, puree) was allowed between days 10 and 14 for 44.9% of respondents, and a free diet was allowed after day 15 for 60.8% of respondents (**Figure 3**). Significant differences were found between geographical areas since a greater proportion of respondents in Africa and Oceania allowed early oral feeding between days 1 and 6 as compared to the rest of the world (**figure 4 and table 3**). We compared these feeding delays to those practiced in the case of salvage TL after prior radiotherapy without pharyngectomy and with primary mucosal closure (case 2); in the case of TL associated with pharyngectomy for a tumor involving the hypopharynx and without prior radiotherapy with the use a pedicled or free flap for reconstruction of mucosal defect of the pharynx (case 3); and in the case of salvage TL associated with pharyngectomy for a tumor involving the hypopharynx, after prior radiotherapy with the use a pedicled or free flap for reconstruction of mucosal defect of the pharynx (case 4). In these last three scenarios, the time period to initiation of oral feeding was significantly delayed compared to case 1 (**Figure 3**). We asked participants which specific factors would lead them to routinely postpone oral intake after TL, even in the absence of postoperative complications. These factors included prior radiotherapy in 65.8%, prior radiotherapy associated with chemotherapy in 57.9%, the use a pedicled or free flap for reconstruction of a mucosal defect of the pharynx in 44.6%, general comorbidities such as diabetes mellitus in 21.9%, advanced age in 8.3%, concurrent neck dissection in 6.5%, voice prosthesis insertion during the same procedure in 5.8%, prior tracheotomy in 4.7%, and anticoagulation therapy in 1.8%. Seventeen participants did not select any of the proposed items.

Characteristics	N-AM n = 23	S-AM n = 65	EU n = 98	AF n = 21	ME/N-AF n = 15	AS n = 46	OC n = 10	p-value
Water	6 (26.1%)	18 (27.7%)	11 (11.2%)	9 (42.9%)	5 (33.3%)	7 (15.2%)	5 (50%)	0.003
Liquid	3 (13%)	9 (13.8%)	3 (3.1%)	8 (38.1%)	1 (6.7%)	4 (8.7%)	4 (40%)	<0.001
Semi solid	0 (0%)	3 (4.6%)	3 (3.1%)	4 (19%)	0 (0%)	2 (4.3%)	2 (20%)	0.033
Free	0 (0%)	3 (4.6%)	1 (1%)	3 (14.3%)	0 (0%)	0 (0%)	1 (10%)	0.024

Table 3. Initiation of oral feeds before day 6 for a patient who underwent TL without pharyngectomy and without prior radiotherapy and with primary mucosal closure (case 1) depending on geographic area

The analysis of time to the initiation of oral feeding showed no significant difference between teams performing fewer than 10 TL per year and those performing more than 10 per year (**figure 5A**). We also found no difference for salvage surgery between respondents performing more than 25% of salvage surgery and those performing less than 25% (**figure 5B**). Time to the initiation of oral feeding was not different between respondents reporting less than 10% rates of PCF and those reporting more than 10% (**figure 5C**). Finally, respondents discharging patients within the first 14 days postoperatively were more likely to allow oral intake before day 10 than those keeping patients in hospital for more than 14 days, regardless of the type of oral intake considered (**figure 5D**).

DISCUSSION

The main interest of our study is that it is an international survey that gathered 278 responses from surgeons practicing in different types of institutions, performing a varying number of total laryngectomies each year, including varying proportions of salvage surgery, from 59 different countries. Our study is therefore the result of a global survey which investigated the protocols of feeding initiation after TL as applied in general practice across the world.

The postoperative management of TL remains controversial, especially with regards to the initiation of oral feeds. The practice of early oral feeding following TL, specifically, is not widely accepted despite increasing evidence in support thereof. In recent years, a growing number of publications indicated that an early resumption of feeding in the first 7 days after surgery is safe practice that would not increase the risk of PCF and would improve the patient's quality of life. Furthermore, it avoids the initial or prolonged use of a nasogastric tube, and reduces the duration of hospitalization and the costs of management.¹⁷⁻²¹ The main argument advanced in these publications is that, due to the continuous production of saliva, the pharyngeal mucosa is never really in a resting state, and due to its acidic pH and the presence of amylase, saliva could be more damaging to the sutures than water or food. Confirming this viewpoint, a recently published study showed that early oral hydration with water on the second postoperative day significantly reduced the rate of PCF.²² The use of a nasogastric tube is also often considered uncomfortable by patients and could be the cause of PCF by exerting continuous pressure on the sutures and by promoting gastro-esophageal reflux.^{17-21,23} However, our survey shows that the use of a nasogastric tube is the most commonly used modality with regards to postoperative feeding after TL due to its use by 96.8% of the respondents. Two meta-analyses published in 2015 and 2021 confirmed that the resumption of oral feeding within the first 5 days did not increase the incidence of PCF.^{24,25} However, these results must be

interpreted with caution because the majority of the studies analyzed did not include patient cohorts which are at a greater risk of developing complications, including those who underwent salvage surgery after radio(chemo)therapy, or following extensive surgery with the requirement for free or pedicled flap reconstruction. Our study also shows that the proportion of teams frequently performing salvage surgery after initial treatment with radio(chemo)therapy varies significantly according to geographic area. It seems that laryngeal preservation protocols are more common in North America, Europe and Oceania, while surgery is more important as first-line treatment in Africa, Middle East, Asia and South America. Boyce and Meyers had shown in 1989 that 84.5% of surgeons waited until at least the 7th day to initiate oral feeding; this delay was postponed to more than 3 weeks for 65% of the surgeons in cases of prior radiation therapy.²⁶ Our study shows that, in current practice, 78.1% of the respondents still wait at least until the 7th postoperative day before initiating water, while more than 85% wait at least until the 7th day before allowing liquids, mixed or free feeding protocols, and even prolonging the delay in initiating feeding in cases of previous irradiation or flap reconstruction. We also observed that a greater proportion of respondents in Africa and Oceania allowed early oral feeding between days 1 and 6 compared to the rest of the world. For Oceania, we could not explain this. Explanation for early feeding in Africa could be that the majority of head and neck surgeons in Sub-Saharan Africa underwent head and neck fellowship training at the University of Cape Town in South-Africa where early feeding protocol is used.²⁷ We found no difference in the time to resumption of feeding based on the volume of surgeries performed each year, suggesting that respondents performing TL very regularly do not allow feeding earlier or later than those with less volumes. We did not find any difference in the delay of resumption of oral feeding according to the reported rate of PCF, which may be in line with studies stating that an early oral feeding does not induce an increased risk of PCF. Our findings regarding complication rates should be considered with caution since these were only reported rates that

could not be verified. These differences may possibly be explained by the lower proportion of salvage surgery performed in countries reporting lower PCF rates since our analysis showed that respondents performing a higher proportion of salvage surgery after radiotherapy reported higher complication rates. Finally, our study shows that respondents authorizing the discharge of their patients within the first 14 days allow oral feeding before the 10th day more frequently than others. These results seem to be in line with studies suggesting that early oral feeding is associated with a reduction in the length of hospital stay, despite the lack of any proven causal link. Indeed, it remains to be determined whether the resumption of feeding is really a limiting factor in authorizing the patient's discharge. In our study, we noted differences in the length of hospitalization depending on the geographical area, suggesting that other factors may be involved when allowing a patient to return home.

CONCLUSION

Despite increasing evidence to support early oral feeding following TL, the majority of respondents prefer to delay the initiation of oral feeding until at least 7 days after surgery. The duration of delay is longer in cases of salvage surgery after radiotherapy, or following total pharyngo-laryngectomy with reconstruction. The overall advantages of early oral feeding and the selection of patients who can benefit from it require further evaluation.

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Legends for figures

Fig 1. Geographic distribution of respondents

Fig 2. Facilities distribution according to geographical area

Fig 3. Time to postoperative initiation of oral feeds in the 4 scenarios

Fig 4. Time to postoperative initiation of semi solid food (mixed, puree) for a patient who underwent TL without pharyngectomy and without prior radiotherapy and with primary mucosal closure (case 1) depending on geographic area.

Fig 5. (A)Time to start oral feeding depending on the number of procedures, (B)time to start oral feeding after salvage TL depending on the proportion of salvage TL performed every yea, (C) time to start oral feeding depending on PCF rate, (D) time to start oral feeding depending on the duration of hospital stay

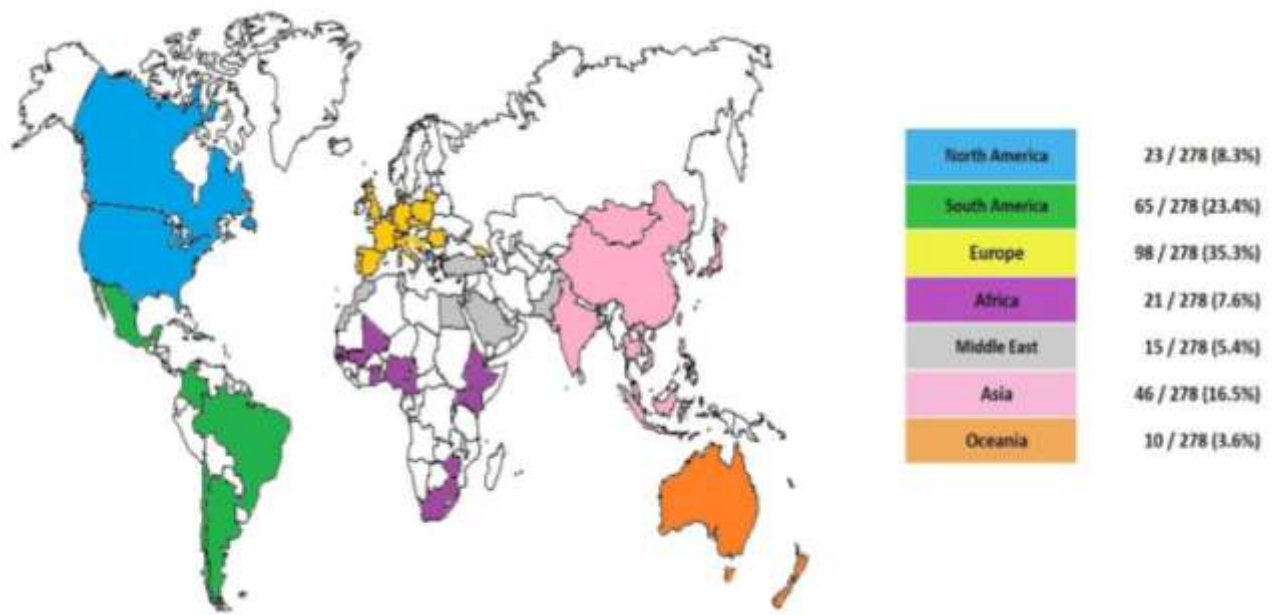


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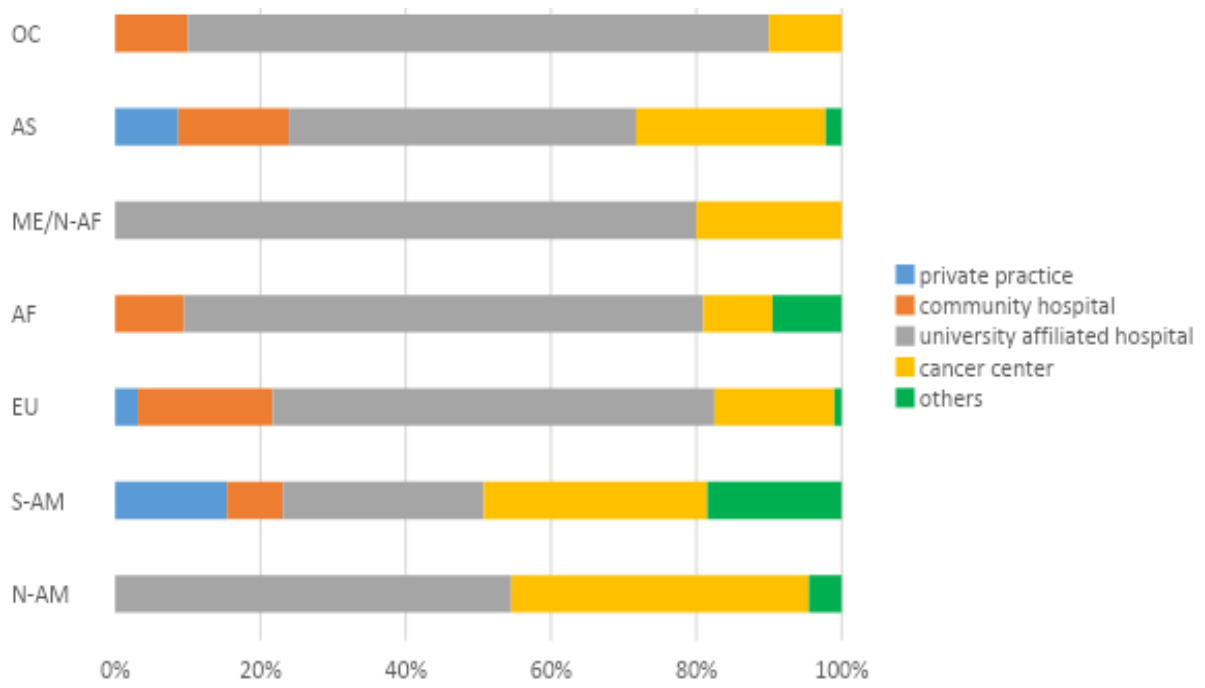


Fig 2. Facilities distribution according to geographical area

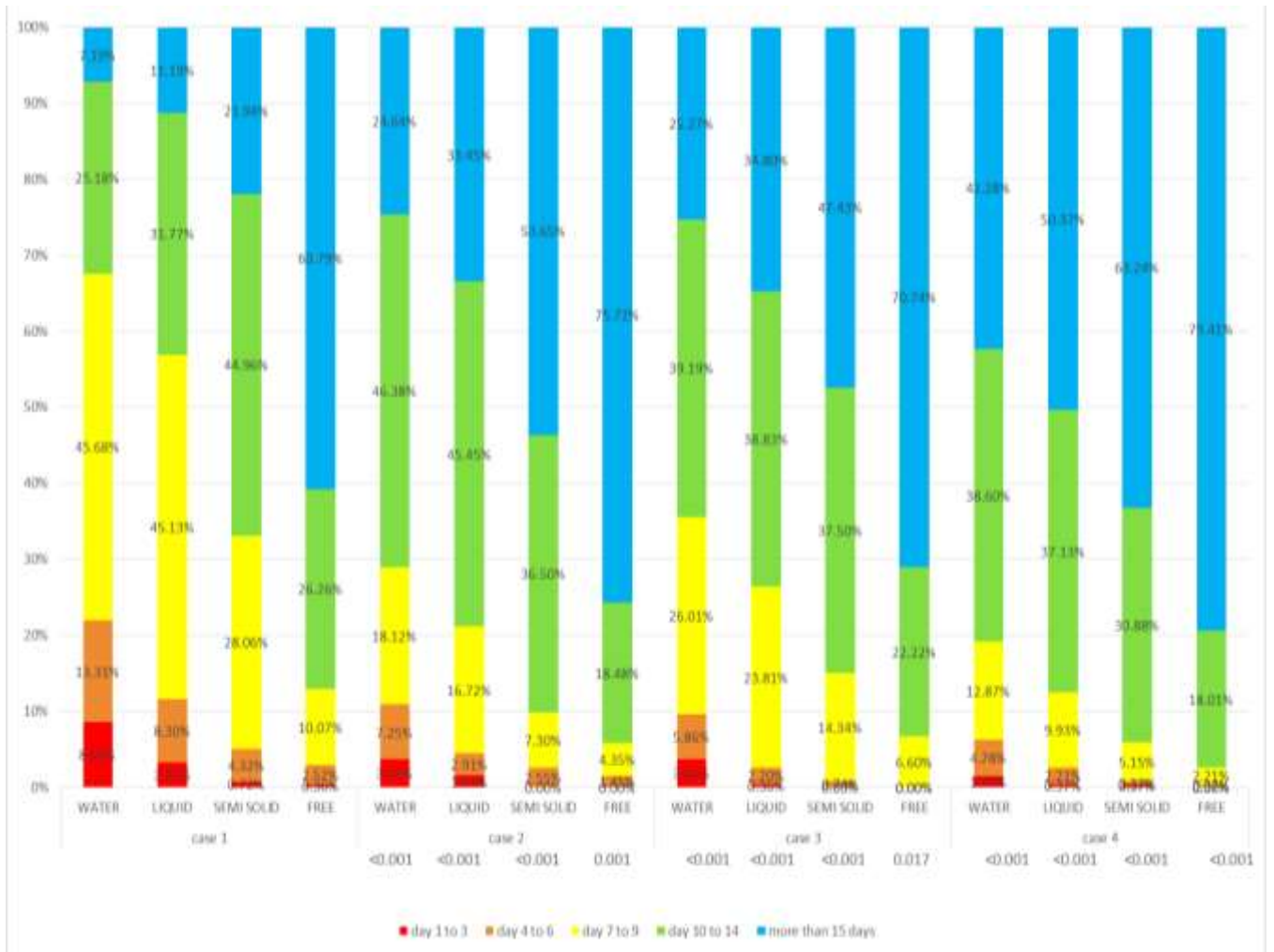


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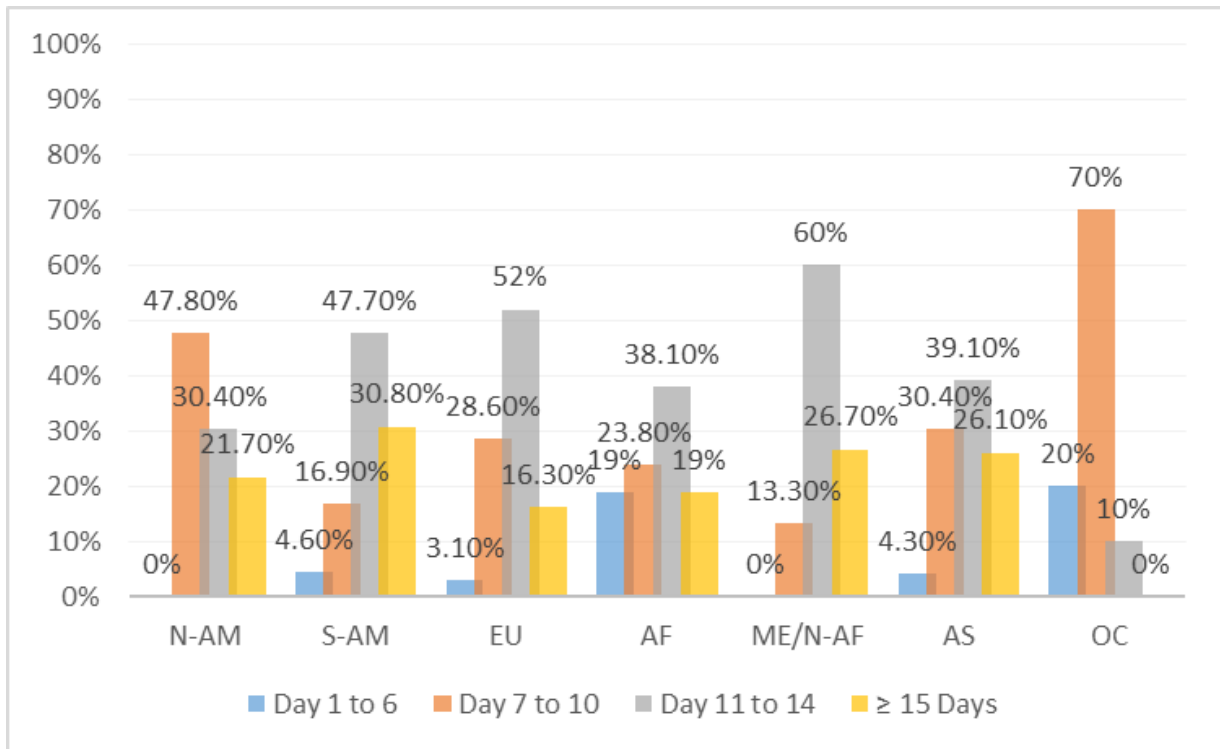


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