

Original Article



Evaluation of perioperative management of advanced ovarian (tubal/peritoneal) cancer patients: a survey from MITO-MaNGO Groups

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ABSTRACT

Objective: The European Society of Gynaecological Oncology (ESGO)-quality indicators (QIs) for advanced ovarian cancer (AOC) have been assessed only by few Italian centers, and data are not available on the proportion of centers reaching the score considered for a satisfactory surgical management. There is great consensus that the Enhanced Recovery After Surgery (ERAS) approach is beneficial, but there is paucity of data concerning its application in AOC. This survey was aimed at gathering detailed information on perioperative management of AOC patients within MITO-MaNGO Groups.

Methods: A 66-item questionnaire, covering ESGO-QIs for AOC and ERAS items, was sent to MITO/MaNGO centers reporting to operate >20 AOC/year.

Results: Thirty/34 questionnaires were analyzed. The median ESGO-QIs score was 31.5, with 50% of centers resulting with a score ≥ 32 which provides satisfactory surgical management. The rates of concordance with ERAS guidelines were 46.6%, 74.1%, and 60.7%, respectively, for pre-operative, intra-operative, and post-operative items. The proportion of overall agreement was 61.3%, and with strong recommendations was 63.1%. Pre-operative diet, fasting/bowel preparation, correction of anaemia, post-operative feeding and early mobilization were the most controversial. A significant positive correlation was found between ESGO-QIs score and adherence to ERAS recommendations.

Conclusion: This survey reveals a satisfactory surgical management in only half of the centers, and an at least sufficient adherence to ERAS recommendations. Higher the ESGO-QIs score stronger the adherence to ERAS recommendations, underlining the correlations between case volume, appropriate peri-operative management and quality of surgery. The present study is a first step to build a structured platform for harmonization within MITO-MaNGO networks.

Keywords: Ovarian Neoplasms; Perioperative Care; Enhanced Recovery After Surgery

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

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Synopsis

1. The ESGO-QIs for AOC have been assessed only by few Italian centers.
2. Only 50% of centers reach ESGO-QIs considered satisfactory for AOC surgical management.
3. There is paucity of data concerning the application of ERAS approach in AOC.
4. Overall agreement with the ERAS guidelines was 61.3%, and with strong recommendations was 63.1%.

INTRODUCTION

Ovarian cancer is diagnosed at an advanced stage in most cases, and, in these conditions, still represents a clinical challenge. Surgery is complex, very frequently involving the upper abdomen and often requiring an extensive approach to the pelvis. Not only surgery, however, needs for skilled equipes, but also the pre- and post-operative management implies experienced care providers, validated algorithms in dedicated structures.

The European Society of Gynaecological Oncology (ESGO) developed a list of quality indicators (QIs) for advanced ovarian (tubal/peritoneal) cancer (AOC) surgery with the aim of helping and auditing clinical practice [1]. The QIs and proposed targets are based on the standards of practice determined from scientific evidence and/or expert consensus. These QIs give practitioners and health administrators a quantitative basis for improving care and organizational processes. Moreover, Enhanced Recovery After Surgery (ERAS) is currently considered as a global surgical quality improvement initiative that results in both clinical improvements and cost benefits to the healthcare system. In particular, the ERAS Society tried to develop guidelines for cytoreductive surgery by structured review of the most recent evidence and by use of a standardised approach [2,3].

The ESGO QIs have been formally assessed only by a minority of centers belonging to the two Italian gynecological oncology networks (MITO, Multicentre Italian Trials in Ovarian Cancer and Gynecologic Malignancies; MaNGO, Mario Negri Gynecologic Oncology). Furthermore, data are not available on the proportion of centers actually reaching the minimal score considered for a satisfactory AOC surgical management. Again, although there is a great consensus by clinicians that the implementation of the ERAS approach is beneficial for surgical patients, there is a paucity of data concerning its application in AOC patients.

The present paper reports on a survey conducted within the MITO and MaNGO networks with the aim to provide a reliable picture of the current peri-operative management of AOC patients in Italy. Data recruited will help for defining a MITO-MaNGO algorithm finalized to health care harmonization, and should be established and incorporated into the Groups' action strategies.

MATERIALS AND METHODS

This survey project was approved by the board of the MITO group on September 2020, it was approved by the MaNGO group assembly on December 21, 2020, and subsequently endorsed by the MaNGO group in January 2021.

The survey was designed to gather detailed information on current perioperative management of AOC patients within MITO/MaNGO Groups. A multiple-choice questionnaire was developed. The questions were selected based on a review of all relevant publications about ERAS and fast-track surgery, and surgical QIs in AOC by an interdisciplinary team with high experience on this field (2 gynecological oncologists, 2 anesthesiologists, 2 medical oncologists).

A 66-item questionnaire was sent to the responsible for each MITO/MaNGO major (based on overall case volume) center (n=38). Each center was asked for: i) filling in the questionnaire involving the physicians responsible for surgery, anesthesiology/intensive care unit, and medical oncology; ii) returning the questionnaires by March 31, 2021. Thirty-four out of 38 (89.4%) sent back the questionnaire. Only questionnaires from centers reporting to operate at least 20 primary AOC per year were considered for the present analysis.

In accordance with Declaration of Helsinki, the present analysis was exempt from formal Institutional Review Boards approval.

Data were collected on: institution-related characteristics (type of center; AOC case volume; annual proportion of primary AOC undergoing upfront cytoreductive surgery and rate of complete tumor resection in primary debulking surgeries; proportion of surgical interventions for AOC performed by dedicated gynecologists/surgeons); methods for evaluating patient fitness for cytoreductive surgery (operability) and for preoperative optimization of patients; pre-operative imaging/clinical score and diagnostic laparoscopy to assess dissemination status and resectability; pre-/intra-/post-operative management covering the ERAS items for perioperative care in cytoreductive surgery. The questionnaire is provided in full in the online supplementary appendix.

Survey main outcomes were presented and compared with i) QIs for AOC surgery developed by the ESGO (each item is associated with a score, the sum of the individual maximum scores being 40; institutions meeting a score of 32 were considered providing a satisfactory surgical management of AOC) [1]; ii) recommendations from the ERAS Society [2,3].

Statistical analysis was performed with Statistical Package for Social Science (SPSS) software version 21.0 (Armonk, NY, USA). Categorical and continuous variables were reported as frequency and percentage and as median and range, respectively. Replies were compared using the Fischer's exact test and the χ^2 test, if needed. Pearson's correlation test was used to determine the association between ESGO QIs final score and adherence to ERAS components. All p-values were two-sided, and statistical significance was set at $p < 0.05$.

RESULTS

We analyzed 30/34 (88.2%) questionnaires from eligible centers: 26 from MITO and 4 from MaNGO group. Most centers (21; 70%) were University Hospitals or Cancer Institutes. Nineteen centers (63.3%) reported that a cancer network (including ovarian cancer) was already active in their own regions, and 17 (56.6%) of them declared to be included among centers where AOC patients are referred to. The large majority (83.3%) declared to submit more than 50% of primary AOC to upfront cytoreductive surgery, 64% of them achieving $\geq 65\%$ complete resection rate. All the centers submitting less than 50% of patients to upfront surgery declared $\geq 65\%$ complete resection.

Table 1 shows further information on the overall management of patients according to the 10 ESGO QIs for AOC surgery. The median score was 31.5 (range: 15–40), with 50% of centers resulting with a score ≥ 32 . There was no evidence for significant difference in the scores by geographic distribution (northern vs central vs southern centers). In particular, most respondents reported a $>65\%$ complete resection rate in primary debulking surgeries, and a $>90\%$ of surgical interventions performed by a gynecologic oncologist, or, however, by a surgeon specifically dedicated to gynecological cancer. A structured algorithm has been established with respect to the evaluation of operability (patient fitness for cytoreductive surgery) and resectability (evaluation of surgical cytoreduction) in 22 (73.3%) and 27 (90%) centers, respectively.

Pre-operative patient management is detailed in **Table 2**. About half of respondents stated not to consider age (43.3%) and hypoalbuminemia (50%) to evaluate patient operability. The large majority (80%) reported to investigate pre-operative anemia with only red blood cell count and hemoglobin value. In particular, only 10% of centers stated prescribing supplementation of Fe, B12 and folates in case of hemoglobin levels <12 g/dL. The ASA score is considered as the key parameter for operability assessment by only 2 (6.7%) respondents. Five centers (16.7%)

Table 1. Quality indicators for advanced ovarian (tubal/peritoneal) cancer surgery

Items	Values (n=30)
Number of surgeries performed per year	
≥ 20	17 (53.3)
≥ 50	9 (33.3)
≥ 100	4 (13.3)
Complete resection rate	
$\leq 50\%$	2 (6.7)
51%–60%	7 (23.3)
$>65\%$	21 (70)
Surgery performed by a dedicated gynecologist/surgeon	
$<90\%$	3 (10)
$\geq 90\%$	27 (90)
Center participating in clinical trials in gynecologic oncology	
No	7 (23.3)
Yes	23 (76.7)
Treatment planned and reviewed at a multidisciplinary team meeting	
No	0 (0)
Yes	30 (100)
Required pre-operative work-up according to ESGO [1]	
No	0 (0)
Yes	30 (100)
Structured reporting of intra-operative findings/surgical procedures/residual disease	
No	2 (6.7)
Yes	28 (93.3)
Availability of pre-/intra-/post-operative management protocol formally implemented for AOC	
No	6 (20)
Yes	24 (80)
Appropriate pathology reports [4]	
$<90\%$	0 (0)
$\geq 90\%$	30 (100)
Structured prospective reporting of postoperative complications	
No	10 (33.3)
Yes	20 (66.7)
Final score according to ESGO quality criteria, median [range]	31.5 [15–40]
<32	15 (50)
≥ 32	15 (50)

Values are presented as number (%).

AOC, advanced ovarian cancer; ESGO, European Society of Gynaecological Oncology.

Table 2. Pre-operative management

Items	Values (n=30)
Evaluation of operability	
Age	
Not considered for the assessment of operability	13 (43.3)
The cut-off of 75 years is adopted for the inclusion of the GVS	10 (33.3)
The cut-off of 70 years is adopted for stratification of anesthesiological risk	7 (23.3)
Pre-operative <3 g/dL albumin serum level	
Not considered for the assessment of operability	15 (50)
Considered predictive of higher rate of complications, and possibly supplemented	15 (50)
Preoperative anemia is investigated with	
Red blood cell count and hemoglobin value	24 (80)
Red blood cell count, hemoglobin value and iron status	6 (20)
ASA score is considered	
The key parameter for operability assessment	2 (6.7)
One of the parameters for operability assessment	28 (93.3)
Radiological Aletti's and/or PCI scores are used for the assessment of patient operability	
No	25 (83.3)
Yes	5 (16.7)
Psychological intervention routinely provided	
No	13 (43.3)
Yes	17 (56.7)
Evaluation of resectability	
Use of pre-operative score for the evaluation of surgical resectability	
No	16 (53.3)
Radiological Aletti's score	3 (10)
Radiological PCI score	4 (13.3)
Both radiological Aletti's and PCI scores	7 (23.3)
Laparoscopy included into the evaluation process of surgical resectability	
No	4 (13.3)
Yes, routinely	13 (43.3)
Yes, in selected cases only	13 (43.3)
Patients undergoing cytoreductive surgery	
1–3 weeks preoperative	
Bowel preparation	22 (73.3)
No	8 (26.7)
Yes, laxatives	
LMWH antithrombotic prophylaxis	7 (23.3)
No	18 (60)
Yes, based on the assessment of VTE risk	5 (16.7)
Yes, routinely	
Tailored diet	25 (83.3)
No	5 (16.7)
Yes	
Preoperative (day before) MBP	
No	3 (10)
Yes, routinely	12 (40)
Yes, only in case of high risk of bowel surgery	15 (50)
Preoperative (1–7 days before surgery) OA in case of high risk of bowel surgery	
No	28 (93.3)
Yes, oral metronidazole/cephalosporine	2 (6.7)
During the 8 h before the intervention	
Absolute fasting	15 (50)
Only clear fluids until 6 hr	6 (20)
Only clear fluids until 2 hr	4 (13.3)
Light meal until 6 hr, clear fluids including oral carbohydrate drinks until 2 hr	5 (16.7)

Values are presented as number (%).

GVS, geriatric vulnerability score; LMWH, low molecular weight heparin; MBP, mechanical bowel preparation; OA, oral antibiotics; PCI, peritoneal cancer index; VTE, venous thromboembolism.

declared to use radiological Aletti's [5] and/or peritoneal cancer index (PCI) [6] scores for the assessment of patient operability, and 14 (46.6%) for the pre-operative evaluation of surgical resectability. A structured report for the radiological evaluation of resectability as well as a routine laparoscopy are implemented by less than half (43.3%) of centers.

In patients undergoing cytoreductive surgery, a tailored (based on a nutritional consultation routinely provided) diet and routine antithrombotic prophylaxis (low molecular weight heparin) in the 1–3 weeks before surgery are adopted by 16.7% of centers. In case of high risk of bowel surgery, almost all centers (93.3%) do not prescribe preoperative antibiotics, while half of them give a (on the day before surgery) bowel preparation with saline osmotic solution in most cases. Fifty percent of centers do not observe absolute fasting during the 8 hours before the intervention, and 16.7% allow a light meal until 6 hours and clear fluids including oral carbohydrate drinks until 2 hours.

Intra-operative management is described in **Table 3**. About the anesthesia management, the majority (83.3%) of centers follow a preoperative protocol for multimodal analgesia. More than half (60%) of the centers use sedatives/anxiolytics. A gastric tube is routinely positioned in 86.6% of centers, one-fourth of which using an intra-operative (oro-gastric) tube. Mechanical prophylaxis of VTE (with stockings or pneumatic compression devices) is routinely adopted in most centers (86.6%). Single antibiotic (cephalosporine) prophylaxis is adopted by 86.6% of centers, except for patients undergoing bowel surgery. During the intraoperative phase, the anesthetic protocol provides the use of epidural analgesia (for >72 hours after surgery), and multimodal analgesia in 83.3% and 70% of centers, respectively. The protective ventilation is guaranteed in 83.3%, and a cardiac output monitoring in approximately most of the centers (93.3%). Deep neuromuscular blockade and use of specific antagonists/reversal are reported by two-thirds (66.6%) of the centers. The fluid therapy is guided by advanced monitoring in 63.3%. Furthermore, prevention of intraoperative hypothermia, and glycaemic control are almost always performed (93.3% and 80%, respectively). In case of large bowel resection, in 90% of centers a temporary protective ileostomy is made in selected cases: in frailty patients (22.2%), when more than one resection is performed (18.5%), and in both the conditions above (59.2%). Protective ileostomy is usually closed after the end of chemotherapy (sixth cycle) in most centers (80%). Peritoneal drain(s) is (are) routinely positioned at the end of surgery by one-third of respondents (33.3%). In about 60% of centers peritoneal drains are positioned in selected cases only: splenectomy/pancreasectomy (100%), bowel surgery (94.1%), liver resection (76.4%), urinary tract surgery (70.5%), diaphragmatic resection/extensive abdominal peritonectomy (47%).

Post-operative management is described in **Table 4**. During the first 24 hours from surgery, patients are admitted to the intensive care unit or monitored at the post-operative care unit in the 66.7% of centers. In the majority of centers (73.3%) fluid re-uptake is allowed after 6–12 hours from surgery, and in less than 20% only after gas passing. Again, oral feeding is allowed after 6–12 hours from surgery in most cases (70%), and in 26.7% only after gas passing. In case of bowel surgery, oral feeding is permitted only after gas passing in about half of centers. Patients are mobilized the day after surgery in all but one centers. The urinary catheter is removed within 48 hours from surgery in 83.3% of centers. Peritoneal drains are removed at the time of gas passing or in the 2nd/3rd post-operative day in most centers. Pharmacological thromboprophylaxis is routinely provided and prescribed for 4 weeks from surgery in most cases (83.3%). Hospital discharge is usually (83.3%) planned 5–7 days after surgery.

Table 3. Intra-operative management

Items	Values (n=30)
CVC routinely positioned	
Yes	12 (40)
No	18 (60)
Gastric tube routinely positioned	
Yes	26 (86.6)
No	4 (13.3)
Mechanical prophylaxis of VTE routinely adopted	
Yes	26 (86.6)
No	4 (13.3)
Measures preventing intraoperative hypothermia routinely adopted	
Yes	28 (93.3)
No	2 (6.7)
Antibiotic prophylaxis (excluding patients undergoing bowel surgery)	
Cephalosporine	26 (86.6)
Cephalosporine + metronidazole	4 (13.3)
Skin preparation with	
Chlorhexidine-alcohol	19 (63.3)
Povidone-iodine	11 (36.7)
Opioid management	
Opioid sparing	17 (56.7)
Opioid free	3 (10)
Opioid liberal	10 (33.3)
Fluid management	
Goal-directed	19 (63.3)
Restrictive	1 (3.3)
Liberal	10 (33.3)
Peritoneal drain(s) positioned at the end of surgery	
No	3 (10)
Yes, routinely	10 (33.3)
Yes, in selected cases only	17 (56.7)
Subcutaneous drain positioned at the end of surgery	
No	20 (66.7)
Yes, routinely	1 (3.3)
Yes, in selected cases only	9 (30)
Postoperative analgesia	
Epidural analgesia performed	
Never	1 (3.3)
Yes, <50% of cases	7 (23.3)
Yes, >50% of cases	10 (33.3)
Yes, routinely	12 (40)
Ultrasound-guided block (e.g. TAP block) routinely performed	
Yes	10 (33.3)
No	20 (66.7)
Surgical wound infiltrated with local anaesthetics	
No	5 (16.7)
Yes, routinely	10 (33.3)
Yes, in selected cases only	15 (50)

Values are presented as number (%).

CVC, central venous catheter; TAP, transversus abdominis plane; VTE, venous thromboembolism.

The rates of concordance with the ERAS guidelines (expressed by the total number of answers in agreement with ERAS recommendations/total number items x total number of centers) were 46.6%, 74.1%, and 60.7%, respectively, for pre-operative, intra-operative, and post-operative items. The proportion of overall agreement was 61.3%, and with strong recommendations was 63.1% (**Table 5**). In particular, the rate of agreement with strong recommendations was 35.5%, 80.8%, and 67.2%, respectively, for pre-operative, intra-operative, and post-operative items. Pearson's correlation test showed a significant positive

Table 4. Post-operative management

Items	Values (n=30)
During the first 24 hr from surgery, is usually managed in	
Intensive care unit	8 (26.7)
Post-operative care unit	12 (40)
Ward	10 (33.3)
Post-operative pain routinely monitored	
Yes	26 (86.6)
No	4 (13.3)
Antibiotic therapy	
No, except for pts submitted to bowel resection(s)	21 (70)
Yes	9 (30)
Fluid reuptake	
Direct after surgery	2 (6.7)
In 6 hr	1 (3.3)
In 6–12 hr	11 (36.7)
>12 hr	11 (36.7)
Only after gas passing	5 (16.7)
Oral feeding in patients	
Not undergoing bowel surgery	
In 6 hr	1 (3.3)
In 6–12 hr	5 (16.7)
>12 hr	16 (53.3)
Only after gas passing	8 (26.7)
Undergoing bowel surgery	
In 6 hr	1 (3.3)
In 6–12 hr	2 (6.7)
>12 hr	8 (26.7)
Only after gas passing	16 (53.3)
Only after feces passing	3 (10)
Mobilization	
The day of surgery	0 (0)
The day after surgery	29 (96.7)
Two days after surgery	1 (3.3)
Removal of urinary catheter	
The day after surgery	14 (46.7)
Two days after surgery	11 (36.7)
At the time of gas passing	5 (16.7)
Removal of gastric tube	
At the end of surgery	16 (53.3)
Within the first 12–24 hr	11 (36.7)
At the time of gas passing	3 (10)
Removal of peritoneal drain(s)	
If positioned because of bowel surgery	
At the time of gas passing	18 (60)
At the time of feces passing	12 (40)
If positioned for reasons other than bowel surgery	
Within 24 hr	7 (23.3)
In 2–3 days	19 (63.3)
In 4–5 days	3 (10)
>5 days	1 (3.3)
Pharmacological thromboprophylaxis	
For 2 wk from surgery	1 (3.3)
For 3 wk from surgery	4 (13.3)
For 4 wk from surgery	25 (83.3)
Hospital discharge is usually planned	
The day after feces passing	1 (3.3)
5–7 days after surgery	25 (83.3)
8–10 days after surgery	4 (13.3)

Values are presented as number (%).

Table 5. Survey outcomes compared with the recommendations from the ERAS Society

Recommendations from ERAS Society [2,3]	Recommendation strength	Centers responding in accordance with the recommendation
Preoperative phase		
Preadmission information, education and counselling (including alcohol/smoking cessation and physical exercise/prehabilitation programs)	Strong positive	17 (56.7)
Preoperative anemia (Hb <12 g/dL): need for screening and treatment	Strong positive	3 (10)
Nutritional screening (supplementation if needed)	Strong positive	5 (16.6)
Preoperative anaesthetic assessment	Strong positive	11 (36.6)
Assessment of cardiac risk and function, screening for obstructive sleep apnea, complete labs, frailty screening		
Pharmacological thromboprophylaxis started 12 hr prior to surgery	Strong positive	23 (76.6)
Preoperative bowel preparation		
Low risk for intestinal surgery: mechanical bowel preparation	Weak negative	18 (60)
High risk for intestinal surgery: mechanical bowel preparation ± oral antibiotic	Weak positive	15 (50)
Preoperative fasting	Strong positive	5 (16.6)
Light meal until 6 hr, clear fluids including oral carbohydrate drinks until 2 hr		
Pre-anaesthetic medication		
Preoperative multimodal analgesia	Weak positive	25 (83.3)
Sedative/anxiolytics	Weak negative	18 (60)
Intraoperative phase		
Prophylactic antibiotics	Strong positive	30 (100)
Skin preparation by chlorhexidine	Strong positive	19 (63.3)
Anaesthetic protocol		
Epidural analgesia (for >72 hr after surgery)	Strong positive	21 (70)
Multimodal analgesia	Weak positive	25 (83.3)
Protective ventilation	Strong positive	25 (83.3)
Cardiac output monitoring	Strong positive	28 (93.3)
Deep neuromuscular block and reversal by specific antagonists	Weak positive	20 (66.6)
Prevention of intraoperative hypothermia	Strong positive	28 (93.3)
Intraoperative glycaemic control	Strong positive	24 (80)
Advanced monitoring to guide fluid therapy	Strong positive	19 (63.3)
Prophylactic abdominal drains	Weak positive	27 (90)
Prophylactic thoracostomy after diaphragmatic peritonectomy ± full thickness muscle resection	Weak positive	1 (3.3)
Postoperative phase		
Prophylactic nasogastric drainage	Weak negative	16 (53.3)
Avoidance of antibiotic prophylaxis	Weak positive	21 (70)
Early removal of urinary catheter (within the morning of postoperative day 3)	Strong positive	30 (100)
Early oral intake resumption		
Clear liquids on the day of surgery	Strong positive	14 (46.6)
Solid food from postoperative day 1	Strong positive	22 (73.3)
Mobilisation as early as the day of surgery (out of bed)	Strong positive	0 (0)
Post-operative nausea and vomiting		
Use of antiemetic drugs	Strong positive	30 (100)
Total intravenous anaesthesia	Weak positive	6 (20)
Pharmacological thromboprophylaxis until 4 wk after surgery	Strong positive	25 (83.3)

relationship between ESGO QIs final score and adherence to strong recommendations from the ERAS Society ($r=0.5$; $p=0.005$).

DISCUSSION

Perioperative management of AOC patients significantly impacts prognosis, being crucial to achieve the best chance of surgical success, minimizing the risk of complications. High quality surgery is not only dependent on the surgical skill but also on an appropriate clinical care during the pre-, intra-, and post-operative phases. The achievement of a correct perioperative approach requires the definition of algorithms, standardized procedures and

protocols, and appropriate integration of subspecialties. MITO and MaNGO are the two Italian gynecologic oncology networks from which the 30 centers included in this survey were selected according to their case volume. Therefore, these centers can be considered a model representative of the actual management of AOC patients in our country. The median ESGO QIs final score for AOC surgery was 31.5, with only 50% of centers resulting with a score ≥ 32 which provides satisfactory surgical management. The present survey is the first one conducted on a national scale for AOC surgery addressing all the items according to the ERAS guidelines published in 2020 [2,3]. Our results show an overall adherence to components of ERAS of 61.3%, and a significant positive correlation between ESGO QIs final score and adherence to the ERAS Society recommendations.

Most centers (83.3%) declared to submit more than 50% of primary AOC to upfront cytoreductive surgery, 64% of them achieving $\geq 65\%$ complete resection rate. These rates seem to be higher than those generally reported in other nationwide studies. Very recently a French assessment of ESGO QIs showed 23% of upfront cytoreductive surgery in 16 macro-regional institutions authorized for gynecologic cancer surgery, and 25% complete surgical cytoreduction was reported in a nationwide Danish survey on tertiary hospitals [7,8]. Our results, however, come from self-assessed reporting compared with those based on individual patient data in the aforementioned studies [7,8].

Structured algorithms are established for the evaluation of operability and resectability in the large majority of centers. Nevertheless, the median ESGO QIs final score was 31.5, with only 50% of centers resulting with a score providing satisfactory surgical management. This was mostly due to the insufficient case volume per center, with 53.3% of centers reporting between 20 and 50 surgeries per year, underlying the case for further efforts to the centralized care. Such score levels were homogeneous all over the country, but cannot be considered as optimal specifically in a context of a gynecologic oncology national network. Moreover, only 63.3% of centers belong to regions where an oncological network is active, and 56.6% are referral centers for AOC in these regions.

Some gynecologic oncology surveys have been conducted to attempt to describe the uptake of ERAS guidelines on a national or international scale [9-11]. There are very few studies, however, addressing this question for ovarian cancer surgery [12,13]. Our results show an overall adherence to ERAS components of 61.3% and to strong recommendations of 63.1%. In particular, the degree of compliance was different for the topics of pre-operative (46.6%), intra-operative (74.1%), and post-operative (60.7%) phases. Our survey found that ERAS guidelines were well adhered to across several domains, most notably prophylaxis against thromboembolism (pre-operative 73%, intra-operative 86.6%, post-operative 83.3%), preoperative multimodal analgesia (83.3%), intraoperative anaesthetic protocol ($\geq 70\%$ in 6/8 items), post-operative nausea and vomiting control (100%), post-operative pain monitoring (86.6%), no routine post-operative antibiotics (70%), early removal of urinary catheter (83.4% within 48 hours after surgery) and gastric tube (90% within 12–24 hours after surgery). It emerged that most centers follow ad hoc anaesthetic protocols, already from the preoperative phase. As part of these strategies, the use of an epidural catheter is foreseen in over two thirds of the centers. It must be emphasized that this approach allows limiting/abolishing the use of opioids, even in the postoperative phase. On the other hand, the use of sedatives in the preoperative phase remains a concern. Although these drugs can facilitate the execution of minimally invasive maneuvers, molecules with a short half-life and a low dose administration should always be preferred [2]. Moreover, multimodal anaesthesia is

adopted by most centers and remains a key element for the success of an ERAS protocol [2,3]. In high-level of complexity interventions, anaesthesia must be guided by advanced monitoring systems with careful prevention of organ damage. In this survey, advanced cardiac monitoring, and prevention of ventilatory lung injury and hypothermia are objectives sought by the majority of the centers.

There were some practices identified which would be considered to be in contradiction with the ERAS recommendations. Pre-operative diet, fasting and bowel preparation, correction of anaemia, post-operative feeding and early mobilization seem to be the most controversial. A tailored diet is not prescribed in the pre-operative phase by 83.3% of centers. Pre-operative malnutrition is associated with increased post-operative morbidity and mortality and poor oncological outcomes, and routine preoperative nutritional screening is therefore strongly recommended [14]. Patients with malnutrition should benefit of oral or parenteral nutritional supplements during 1–2 week before surgery [2].

Long fasting before elective surgery was usually recommended to avoid full stomach and thus the risk of pulmonary aspiration [15]. On the contrary, it has been proven that fasting from midnight does not reduce gastric content [16], and the ERAS Society recommends to allow a light meal up to 6 hours and non-alcoholic clear fluids up to 2 h before surgery [2]. Only 16.7% of centers adhere to this recommendation, with half of centers still requiring absolute fasting during the 8 hours before the intervention.

The recommendations for bowel preparation are controversial given the conflicting evidence that was generated recently. Only 10% of centers do not use mechanical bowel preparation (MBP), whereas 50% in case of probable bowel surgery. On the other hand, only 6.7% of centers prescribe oral antibiotics (OA) in any case. Currently, there is a lack of appropriate investigations examining bowel preparation within the AOC patients submitted to cytoreductive surgery, and therefore data must be derived from the colorectal literature, which has remained controversial. The most recent Cochrane review supports antibiotic prophylaxis [17], while MBP seems to be equivalent to no preparation and MBP plus OA is equivalent to OA alone [18-20]. In 2019, the MOBILE (Mechanical and oral antibiotic bowel preparation versus no bowel preparation for elective colectomy) study, however, showed no difference between MBP plus OA and no preparation with respect to surgical site infection, anastomotic leak or reoperation rate [21]. It is therefore consistent that only weak recommendations are found for bowel preparation regardless probable intestinal resection.

Treatment of preoperative anaemia (Hb <12 g/dL) is strongly recommended to reduce cardiac events and mortality, but only 10% of centers declared to follow this guideline. Similarly, a discordant management has emerged with respect to early oral intake and mobilization with only a low minority, if any, attempting to follow the ERAS recommendations. If the prompt correction of anaemia could be further implemented through a more adequate information on the benefits from normal Hb levels at the time of cytoreductive surgery, early oral intake and mobilization seem to be related to consolidated practices which can be even more difficult to change. Early oral intake, aiming for clear liquids on the day of surgery and solid food from postoperative day one, in the absence of risk factors for delayed gastric emptying (resection of lesser omentum), reduces the risk of anastomotic dehiscence and improves resumption of bowel function [2,3]. The benefits of early mobilisation in AOC patients, are likely to be similar as those seen in comparable surgeries, while prolonged bed rest is associated with increased risk of pulmonary and thromboembolic complications [2,3].

Overall, our results show an overall adherence to components of ERAS which is relatively consistent with the outcome of an international survey of peri-operative practice on open gynecologic cancer surgery showing 61% of ERAS implementation in Europe [9]. This survey showed a good (>80%) adherence to the ERAS guidelines in the domains of deep vein thrombosis prophylaxis, early removal of urinary catheter after surgery, and early introduction of ambulation, while areas with poor adherence included the use of bowel preparation, adoption of modern fasting guidelines, carbohydrate loading, use of nasogastric tubes and peritoneal drains, intra-operative temperature monitoring, and early feeding. The present survey confirms only some of the above critical areas (i.e. bowel preparation, fasting guidelines, carbohydrate loading, early feeding), showing some improvement in the ERAS guidelines implementation.

From a 2017 survey on the ERAS for AOC in three different European countries, 33% of Italian centers followed a written ERAS protocol [22]. Even though these rates are not correctly comparable due to different ERAS guidelines [2,3,23,24], centers and investigation items, it could be suggested, at large, an improved compliance in a 3-year period from 2017 to the time of the current survey.

Our study shows that higher the ESGO QIs score stronger the adherence to the ERAS Society recommendations. This evidence underlines once more the correlations between case volume, appropriate peri-operative management and quality of surgery.

The major strength of this study is that it is the first conducted on a national scale for AOC including all centers with adequate case volume from the entire gynecologic cancer cooperative network. A limitation of the study relates to the inherent bias and reporting errors intrinsic to the surveys, and we cannot rule out that some results mirror individual rather institutional practices. Centralized care could not only improve the quality of surgery but also facilitate standardization of peri-operative management of AOC. In fact, the present survey still reveals both the insufficient cancer network all over the country and the lack of centralization of surgical care for AOC patients. These are the major factors responsible for non-optimal compliance to the ESGO requirements and ERAS recommendations.

The authors consider the present study a first step to build a consistent structured reporting platform for the MITO-MaNGO gynecological oncology units and facilitate a wide implementation and standardization of ERAS protocol for AOC patients in Italy.

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