EJGO European Journal of Gynaecological Oncology

Omentectomy in endometrial cancer: an evidence-based insight

M.R. Brincat[1], Y. Muscat Baron[2], E. Borg[3]

Department of Obstetrics and Gynaecology, Mater Dei Hospital, Gwardamangia (Malta)

Summary

Omentectomy is the surgical removal of the omentum. It is a routine component of staging surgery for confirmed or suspected ovarian carcinoma; however there is currently no consensus regarding omentectomy in surgery performed for endometrial cancer. Additionally, the extent of omental resection in patients without macroscopic deposits is unclear. A systematic search of PubMed MEDLINE resources was performed using the MeSH terms 'endometrium' 'uterus' 'omentum' 'surgery' 'neoplasms', and 'neoplasm metastasis'. The authors conducted a literature review of articles published through January 2016 to summarize the current evidence analyzing omental assessment in endometrial cancer and the repercussions its involvement could have on patient management and prognosis. Metastasis to the omentum is a significant finding in endometrial cancer cases as it indicates upstaging to Stage IV-B (FIGO 2009). Assessment for omental spread helps indicate whether neoplastic deposits are spread beyond the conventional radiotherapy field and assist decision-taking with regards to platinum therapy. Macroscopic assessment of the omentum at the time of abdominal surgery for endometrial carcinoma has been shown to be highly sensitive and specific, and thus advisable. Omental biopsies and histopathological examination are more likely to affect management planning in cases at high-risk of upstaging, these being poorly differentiated tumors (Grade 2 and above), non-endometroid cytologies, cases with > 50% myometrial invasion, or cervical or adnexal involvement of the tumor. Total omentectomy and thorough histological assessment is superior with regards to detection of neoplastic spread however presents a significant strain on hospital laboratory services. Maximal surgical cytoreduction including omentectomy has been shown to improve overall survival in Stage 3 or 4 patients with good performance status.

Key words: Ovarian carcinoma; Omentum; Endometrial cancer; Evidence-based study.

Introduction

With an incidence of 28.4 per 100,000 women, endometrial cancer is the fourth leading malignancy in women behind breast, lung, and colorectal [1]. The incidence of endometrial carcinoma is on the rise due to increasing life expectancy and improved therapeutic options which are replacing hysterectomy for benign conditions. Endometrial cancer is often diagnosed in the early stages of the disease; 74% of females diagnosed with uterine cancer present at clinical Stage I [2,3]. Early presentation permits timely management with excellent clinical outcome (95.3% five-year survival in Stage 1 disease) (Figure 1) [4-6].

Staging classifications by the International Federation of Obstetrics and Gynaecology (FIGO) were initially based on clinical examination to assess the anatomical extent of the disease; however in 1988 FIGO staging for endometrial cancer changed from a clinical to a surgical one. While surgical staging remains the primary mode for defining the extent of disease, histological grade remains an important prognostic indicator, and is highly predictive in determining propensity for metastasis [7]. Moreover, Type 2 non-endometroid histologies, namely clear cell, papillary serous adenocarcinoma, and carcinosarcoma are associated with a higher risk of extra uterine metastasis and recurrence. For this reason non-endometroid Type 2 carcinomas represent a relatively higher proportion of high-stage disease presentation [8]. Prognosis in serous and clear cell carcinomas has been repeatedly observed to be significantly worse than that of patients with grade 3 poorly-differentiated endometrioid carcinoma [9]. This may reflect different mechanisms of retroperitoneal spread among different histologic subtypes.

The omentum

Endometrial cancer metastasizes by direct spread into the myometrium or cervix, haematogenous dissemination, lymphatic embolisation, and peritoneal seeding [10]. Omental spread is understood to occur as a result of peritoneal seeding and local lymphatic spread [11]. Research published in Clinical Cancer Research also identified biochemical crosstalk between omental adipose stromal cells (O-ASC) and tumor cells. In vitro, O-ASC facilitate neovascularisation and thus survival and progression of endometrial tumor cells [12].

Omentectomy is the surgical removal of the omentum. It is a routine component of staging surgery for confirmed or suspected ovarian carcinoma [13], however there is currently no consensus regarding omentectomy in surgery performed for endometrial cancer [14, 15]. Furthermore, the extent of omentectomy in patients without macroscopic deposits is not clear (total/infracolic omentectomy, or biopsy).

Revised manuscript accepted for publication May 2, 2016

Eur. J. Gynaecol. Oncol. - ISSN: 0392-2936
XXXVIII, n. 4, 2017
doi: 10.12892/ejgo3714.2017

7847050 Canada Inc.
www.irog.net

Stage	Women
Stage I	95.3
Stage II	77.0
Stage III	39.0
Stage IV	13.6
All Stages	84.4
Stage Not Known	54.4

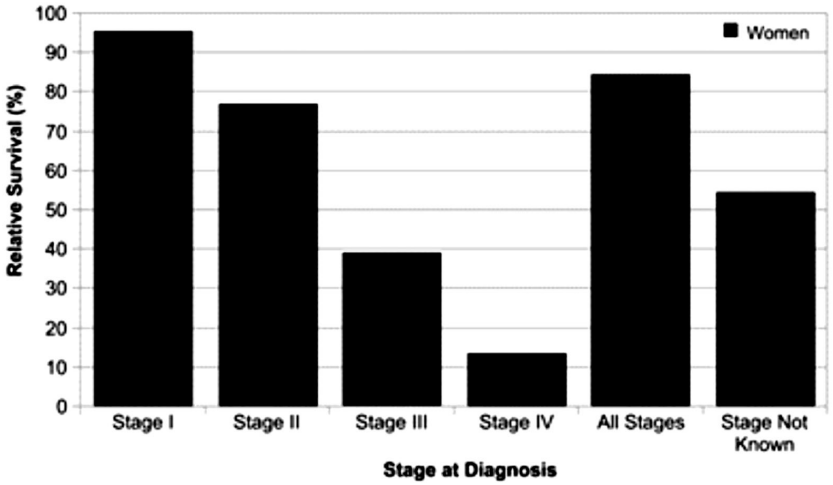

Figure 1. — Five-year relative survival by stage in endometrial carcinoma - Former Anglia Cancer Network [6].

To ensure that any benefit outweighs surgical morbidity, each component of staging surgery must provide therapeutic benefit, either by direct effect on survival or by providing information that aids treatment planning. In contrast to lymphadenectomy, omentectomy or omental biopsies are not thought to add significant morbidity to the surgery [16]. The ASTEC trial has shown that the added morbidity of lymph node dissection for full surgical staging in early endometrial cancer is not justified. This is especially so in view of technological advances and decreased toxicity in adjuvant image-guided radiotherapy [17]. Literature does not specifically quantify omentectomy-related complications in gynaecological procedures, however these are generally regarded to be low. In gastrointestinal and bariatric surgery, the association with splenic and mesocolon injuries [18], as well as increased adhesions [19], have been reported.

The reported frequency of omental metastases in endometrial cancer cases thought preoperatively to be confined to the cavity ranges from 2.4 to 8.3%. Omental micrometastases account for 11-71.4% of this neoplastic spread [19-30]. In a prospective study, Fujiwara *et al.* identified omental involvement in 3% of 134 patients with clinical Stage I endometrioid adenocarcinoma [30]. The omental metastasis rate for these patients was lower than the rate of extrauterine spread to adnexae (7.5%) or lymph nodes (10.2%). Thus, the authors suggested that routine practice of omentectomy as part of staging surgery in endometrial cancer cases may not be efficacious, as most intra-abdominal spread would still be picked up through peritoneal washings and histological examination of the lymph nodes. This may be no longer a reasonable conclusion to make now that practice is moving away from routine pelvic lymphadenectomy due to implications of the ASTEC trial.

Omentectomy or omental biopsies are more frequently performed in cases of serous histology because of the similar pattern of spread to ovarian cancer [31]. Kato *et al.* retrospectively analyzed a series of 30 women with uterine serous carcinoma; eight of the patients had undergone either omental biopsy or omentectomy, with 88% of omental specimens containing malignant cells [32]. Specimens were however not clearly categorized as being either grossly or microscopically involved with metastatic disease. In a similar analysis of 65 women, Geisler *et al.* further confirmed the tendency of this histological subtype for extrauterine spread. Approximately 24% of patients exhibited microscopic omental or peritoneal spread despite negative lymph nodes, and nearly 40% of Stage IV patients were correctly diagnosed only after staging surgery, as that employed for ovarian cancer, was performed [33]. This suggested that more radical surgery is justified for uterine serous carcinoma.

Macroscopic omental assessment

Macroscopic features of omentum appear to be helpful in suspecting the presence of metastasis. Intraoperative inspection and palpation of the omentum has been found to be both sensitive and specific. In a study by Usubütün *et al.*, macroscopic impression was correct in 97.3% of cases of endometrial or ovarian cancer [34]. In another study, macroscopic impression was correct in 97.1% of the cases [35]. Chen *et al.* reported that on pathologic examination of macroscopically-negative specimens, only 1.5% had metastases (three of 202 cases), thus emphasising the robust negative predictive value (NPV) of this technique [36]. Given the metastatic capability of serous endometrial carcinoma, Gehrig *et al.* investigated inspection and sampling in 65 women with uterine serous carcinoma. This method was found to have a sensitivity of 0.89 and a specificity of 1.00 [37]. These findings suggest that when omentum is involved (thereby upstaging the patient to Stage

Stage I[a]	Tumor contained to the corpus uteri		
	IA	No or less than half myometrial invasion	
	IB	Invasion equal to or more than half of the myometrium	
Stage II		Tumor invades the cervical stroma but does not extend beyond the uterus[b]	
Stage III[a]		Local and/or regional spread of tumor[c]	
	IIIA	Tumor invades the serosa of the corpus uteri and/or adnexas	
	IIIB	Vaginal and/or parametrial involvement	
	IIIC	Metastases to pelvis and/or para-aortic lymph nodes	
		IIIC1	Positive pelvic nodes
		IIIC2	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes
Stage IV[a]			Tumor invades bladder and/or bowel mucosa and/or distant metastases
	IVA		Tumor invasion of bladder and/or bowel mucosa
	IVB		Disant metastases, including intra-abdominal metastases and or inguinal lymph nodes

FIGO = International Federation of Gynecology and Obstetrics
[a] Includes grades 1, 2, or 3
[b] Endocervical glandular involvement only should be considered as stage I and no longer as stage II.
[c] Positive cytology has to be reported separately without changing the stage.

Figure 2. — 2009 FIGO staging system for carcinoma of the endometrium.

IV-B disease), spread is generally diagnosed by gross visualization.

In the study of Usubütün *et al.* evaluating 258 cases of ovarian and endometrial carcinomas, it was found that the incidence of metastases in macroscopically-negative omentectomy specimens was actually lower in endometrial carcinoma cases than in ovarian carcinoma cases (0.8% and 4.5% respectively). The authors therefore concluded that in cases where omental deposits would upstage the tumor, careful assessment should be carried out by searching for foci by the naked eye, palpation, and/or dissection. If no macroscopic lesion is detectable in a patient with a high-grade tumor (that will necessitate adjuvant therapy anyway), three to five omental biopsies were suggested for appropriate staging [34].

Extent of omental sampling

The extent of omental sampling in a macroscopically normal omentum is unclear. In a cohort of 811 endometrial cancer patients, Taner *et al.* found that omental micrometastases were detected five times more often with total omentectomy when compared with sampling (11.3% *vs.* 2.1%, $p < 0.001$) [38]. Even if one could detect omental metastases more reliably with total omentectomy, this may not demonstrate the real incidence of omental metastasis due to the limitation of pathologic examination. Detection of micrometastasis in a large omental specimen necessitates a large number of sections in the pathologic examination, increasing the load on hospital histopathology services [39].

Role in staging and patient management

The most logical application of omental sampling is that of defining the true extent of disease. Microscopic and macroscopic omental metastasis signify a poorer prognosis for patients, with two-year overall survival for these groups being very similar (35.7% *vs.* 36.8%, respectively). Two-year disease-free survival (DFS) in patient with any omental metastasis is also poor at 28.2%. This is in part due to the high association of omental metastasis with spread to adnexae (66.7%), lymph nodes (60.5%), cervical stroma (47.9%), and corpus serosa (29.2%) [36]. Omental metastasis is also associated with appendiceal implants [40]. Histologically confirmed extra pelvic disease categorizes the case as Stage IV-B (Figure 2). In such circumstances disease would be outside the conventional field targeted by pelvic external beam radiotherapy or brachytherapy. Administration of a systemic chemotherapeutic agent and radiotherapy may be more appropriate management.

In a prospective study investigating the influence of omental biopsy on adjuvant treatment field in clinical Stage I endometrial carcinoma, Nieto *et al.* found that this procedure affected management in 15% of high-risk patients [26]. These high-risk features were poor tumor differentiation, > 50% myometrial invasion, or cervical/adnexal involvement of the tumor. These are features that can be assessed from preoperative endometrial sampling and radiology (CT/MR). Furthermore, no statistically significant increase in morbidity was observed in low-risk patients undergoing omental biopsy.

Effect of omentectomy on patient outcome

There are very few literature publications addressing the effect of omentectomy on patient outcome in terms of disease-free interval and overall survival, especially in the treatment of clinically early-stage endometrial endometroid adenocarcinoma. Although omentectomy has a role in the detection of omental micrometastases, its direct effect on survival in affected patients is not clear. Evidence is however mostly in favour of maximal surgical cytoreduction (including omentectomy) in Stage III-IV endometrial cancer patients with good performance status [41, 42]. This however does not solely address omentectomy, and other confounders (components of radical surgery) may be at play. In a study by Bristow *et al.* patients who had optimal debulking surgery (residual tumor ≤ one cm in maximal diameter) were found to have a median survival rate of 34.2 months, three times that of patients for whom optimal debulking could not be attained ($p = 0.0001$). Microscopic residual disease also translated into better overall survival when compared to gross disease smaller than one cm [43].

Some authors postulate that apart from helping define the disease stage and manage the patient, omentectomy may provide direct benefit through debulking of possibly undiagnosed deposits. Trials specifically addressing this cytoreductive effect of omentectomy are however not

available in literature due to the complex task of matching patients in terms of age, performance status, extra-abdominal spread, lymph node metastases, adjuvant therapy, and grade.

Conclusion

Macroscopic assessment of the omentum at the time of abdominal surgery for endometrial carcinoma is highly sensitive and specific, and thus advisable. Omental biopsies are more likely to affect management planning in cases at high-risk of upstaging, these being poorly differentiated tumors (Grade 2 and above), non-endometroid cytologies, cases with > 50% myometrial invasion, or cervical or adnexal involvement of the tumor. Pathological assessment of omental biopsies in macroscopically negative specimens help indicate whether tumor deposits are spread beyond the conventional radiotherapy field and assist decision-taking with regards to platinum therapy. Total omentectomy and thorough histological assessment are superior with regards to detection of tumor spread, however present a significant strain on hospital laboratory services. Maximal surgical cytoreduction including omentectomy has been shown to improve overall survival in Stage III or IV patients with good performance status. Total resection is more likely to alter clinical outcome when there is bulkier disease that can be completely removed.

References

[1] Cancer Research UK: "Data Table: Cancer incidence rates in the UK". Available at: http://publications.cancerresearchuk.org/cancerstats/statsincidence/dtincrates.html

[2] Amant F., Moerman P., Neven P., Timmerman D., Van Limbergen E., Vergote I.: "Endometrial cancer". *Lancet*, 2005, *366*, 491.

[3] Cancer Research UK: "Uterine cancer statistics". Available at: http://www.cancerresearchuk.org/health-professional/cancerstatistics/statistics-by-cancer-type/uterine-cancer

[4] Cancer Research UK: Cancer of the body of the uterus (C54): 2006-2010". Available at: http://www.cancerresearchuk.org/sites/default/files/cstream-node/surv_1yr_stage_w_uterus.pdf

[5] Howlader N., Noone A.M., Krapcho M., Garshell J., Miller D., Altekruse S..F, *et al.* (eds): "SEER Cancer Statistics Review, 1975-2012" Bethesda, MD: National Cancer Institute. Available at: http://seer.cancer.gov/archive/csr/1975_2012/

[6] Cancer Research UK: "Cancer of the Body of the Uterus (C54): 2002-2006" Available at: http://www.cancerresearchuk.org/sites/default/files/cstream-node/surv_5yr_stage_w_uterus.pdf

[7] Mendivil A., Schuler K.M., Gehrig P.A.: "Non-endometrioid adenocarcinoma of the uterine corpus: a review of selected histological subtypes". *Cancer Control*, 2009, *16*, 46.

[8] Haltia U.M., Bützow R., Leminen A., Loukovaara M.: "FIGO 1988 versus 2009 staging for endometrial carcinoma: a comparative study on prediction of survival and stage distribution according to histologic subtype". *J. Gynecol. Oncol.*, 2014, *25*, 30.

[9] Hamilton C.A., Cheung M.K., Osann K., Chen L., Teng N.N., Longacre T.A., *et al.*: "Uterine papillary serous and clear cell carcinomas predict for poorer survival compared to grade 3 endometrioid corpus cancers". *Br. J. Cancer*, 2006, *94*, 642.

[10] Creasman W.T., Morrow C.P., Bundy B.N., Homesley H.D., Graham J.E., Heller P.B.: "Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study". *Cancer*, 1987, *60*, 2035.

[11] Freij M.A., Burbos N., Mukhopadhyay D., Lonsdale R., Crocker S., Nietto J.J.: "The role of omental biopsy in endometrial cancer staging". *Gynecol. Surg.*, 2009, *6*, 215.

[12] Klopp A.H., Zhang Y., Solley T., Amaya-Manzanares F., Marini F., Andreeff M., *et al.*: "Omental adipose tissue-derived stromal cells promote vascularization and growth of endometrial tumors".Clin. Cancer Res., 2012, *18*, 771.

[13] Benedet JL., Bender H., Jones H.I., Ngan H.Y., Pecorelli S.: "FIGO staging classifications and clinical practice guidelines in the management of gynecologic cancers. FIGO Committee on Gynecologic Oncology". *Int. J. Gynaecol. Obstet.*, 2000, *70*, 209.

[14] Ben-Shachar I., Pavelka J., Cohn D.E., Copeland L.J., Ramirez N., Manolitsas T., Fowler J.M.: "Surgical staging for patients presenting with grade 1 endometrial carcinoma". *Obstet. Gynecol.*, 2005, *105*, 487.

[15] Dilek S., Dilek U., Dede M., Deveci M.S., Yenen M.C.: "The role of omentectomy and appendectomy during the surgical staging of clinical stage I endometrial cancer". *Int. J. Gynecol. Cancer*, 2006, *16*, 795.

[16] Fujiwara H., Saga Y., Takahashi K., Ohwada M., Enomoto A., Konno R., *et al.*: "Omental metastases in clinical stage I endometrioid adenocarcinoma". *Int. J. Gynecol. Cancer*, 2008, *18*, 165.

[17] ASTEC study group, Kitchener H., Swart A.M., Qian Q., Amos C., Parmar M.K.: "Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study". *Lancet*, 2009, *373*, 125.

[18] Kim D., Lee J., Kim W.: "A comparison of total versus partial omentectomy for advanced gastric cancer in laparoscopic gastrectomy". *World J. Surg. Oncol.*, 2014, *12*, 64.

[19] Ariake K., Yokoyama S., Doi T., Takemura S., Kajiwara T., Kuroda F.: "Effect of omentum removal on the risk for postoperative adhesive small bowel obstruction recurrence: a case-control study". *Int. J. Surg.*, 2015, *13*, 27.

[20] Dilek S., Dilek U., Dede M., Deveci M.S., Yenen M.C.: "The role of omentectomy and appendectomy during the surgical staging of clinical stage I endometrial cancer". *Int. J. Gynecol. Cancer*, 2006, *16*, 795.

[21] Usubütün A., Ozseker H.S., Himmetoglu C., Balci S., Ayhan A.: "Omentectomy for gynecologic cancer: How much sampling is adequate for microscopic examination?" *Arch. Pathol. Lab. Med.*, 2007, *131*, 1578.

[22] Fujiwara H., Saga Y., Takahashi K., Ohwada M., Enomoto A., Konno R., *et al.*: "Omental metastases in clinical stage I endometrioid adenocarcinoma". *Int. J. Gynecol. Cancer*, 2008, *18*, 165.

[23] Freij M.A., Burbos N., Mukhopadhyay D., Lonsdale R., Crocker S., Nietto J.J.: "The role of omental biopsy in endometrial cancer staging". *Gynecol. Surg.*, 2009, *6*, 215.

[24] Metindir J., Dilek G.B.: "The role of omentectomy during the surgical staging in patients with clinical stage I endometrioid adenocarcinoma". *J. Cancer Res. Clin. Oncol.*, 2008, *134*, 1067.

[25] Saygili U., Kavaz S., Altunyurt S., Uslu T., Koyuncuoglu M., Erten O.: "Omentectomy, peritoneal biopsy and appendectomy in patients with clinical stage I endometrial carcinoma". *Int. J. Gynecol. Cancer*, 2001, *11*, 471.

[26] Nieto J.J., Gornall R., Toms E., Clarkson S., Hogston P., Woolas R.P.: "Influence of omental biopsy on adjuvant treatment field in clinical Stage I endometrial carcinoma". *BJOG*, 2002, *109*, 576.

[27] Chen S.S., Spiegel G.: "Stage I endometrial carcinoma. Role of omental biopsy and omentectomy". *J. Reprod. Med.*, 1991, *36*, 627.

[28] Saygili U., Kavaz S., Altunyurt S., Uslu T., Koyuncuoglu M., Erten O.: "Omentectomy, peritoneal biopsy and appendectomy in patients with clinical stage I endometrial carcinoma". *Int. J. Gynecol. Cancer*, 2001, *11*, 471.

[29] Eto T., Saito T., Kasamatsu T., Nakanishi T., Yokota H., Satoh T., *et al.*: "Clinicopathological prognostic factors and the role of cytoreduction in surgical stage IVb endometrial cancer: a retrospective multi-institutional analysis of 248 patients in Japan". *Gynecol. Oncol.*, 2012, *127*, 338.
[30] Fujiwara H., Saga Y., Takahashi K., Ohwada M., Enomoto A., Konno R., *et al.*: "Omental metastases in clinical stage I endometrioid adenocarcinoma". *Int. J. Gynecol. Cancer*, 2008, *18*, 165.
[31] Cirisano F., Robboy S., Dodge R., Bentley R., Krigman H., Synan I., *et al.*: "Epidemiologic and surgicopathologic findings of papillary serous and clear cell endometrial cancers when compared to endometrioid carcinoma". *Gynecol. Oncol.*, 1999, *74*, 385.
[32] Kato D., Ferry J., Goodman A., Sullinger J., Scully R., Goff B., *et al.*: "Uterine papillary serous carcinoma (UPSC): a clinicopathologic study of 30 cases". *Gynecol. Oncol.*, 1995, *59*, 384.
[33] Geisler J., Geisler H., Melton M., Wiemann M.: "What staging surgery should be performed on patients with uterine papillary serous carcinoma?" *Gynecol. Oncol.*, 1999, *74*, 465.
[34] Usubütün A., Ozseker H.S., Himmetoglu C., Balci S., Ayhan A.: "Omentectomy for gynecologic cancer: how much sampling is adequate for microscopic examination?" *Arch. Pathol. Lab. Med.*, 2007, 131, 1578.
[35] Doig T., Monaghan H.: "Sampling the omentum in ovarian neoplasia: when one block is enough". *Int. J. Gynecol. Cancer*, 2006, *16*, 36.
[36] Chen S.: "Extrauterine spread in endometrial carcinoma clinically confined to the uterus". *Gynecol. Oncol.*, 1985, *21*, 23.
[37] Gehrig P.A., Van Le L., Fowler W.C. Jr.: "The role of omentectomy during the surgical staging of uterine serous carcinoma". *Int. J. Gynecol. Cancer*, 2003, *13*, 212.
[38] Turan T., Ureyen I., Karalok A., Tasci T., Ilgin H., Keskin L., *et al.*: "What is the importance of omental metastasis in patients with endometrial cancer?" *J. Turk. Ger. Gynecol. Assoc.*, 2014, *15*, 164.
[39] Nieto J.: "Influence of omental biopsy on adjuvant treatment field in clinical Stage I endometrial carcinoma". *BJOG*, 2002, *109*, 576.
[40] Joo W., Schwartz P., Rutherford T., Seong S., Ku J., Park H., et al.: "Microscopic omental metastasis in clinical Stage I endometrial cancer: a meta-analysis". *Ann. Surg. Oncol.*, 2015, *22*, 3695.
[41] Joint SOGC-GOC-SCC Clinical Practice Guideline No. 289: "The role of surgery in endometrial cancer". Available at: http://sogc.org/wp-content/uploads/2013/07/gui289CPG1304E.pdf
[42] Ueda M.S., Bristow E.R.: "Cytoreductive surgery in endometrial cancer and uterine sarcomas". *In:* Yildirim Y. (ed). *Cytoreductive surgery in gynecologic oncology: a multidisciplinary approach*. 2010, 123. Available at: http://www.trnres.com/ebook/uploads/yildirim/T_1273558229Yildirim-7.pdf
[43] Bristow R., Zerbe M., Rosenshein N., Grumbine F., Montz F.: "Stage IVB endometrial carcinoma: the role of cytoreductive surgery and determinants of survival". *Gynecol. Oncol.*, 2000, *78*, 85.

Corresponding Author:
M.R. BRINCAT, M.D. (Melit), Msc. Rep. Health
Department of Obstetrics and Gynaecology
Mater Dei Hospital
Gwandamangia (Malta)
e-mail: mark.a.brincat@gov.mt