Gynecologic Oncology 148 (2018) 515–520

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Processing of fallopian tube, ovary, and endometrial surgical pathology specimens: A survey of U.S. laboratory practices

Goli Samimi [a,*], Britton Trabert [a], Máire A. Duggan [b], Jennifer L. Robinson [c], Kisha I. Coa [c], Elizabeth Waibel [d], Edna Garcia [d], Lori M. Minasian [a], Mark E. Sherman [e]

[a] National Cancer Institute, Bethesda, MD 20892, USA
[b] Department of Pathology and Laboratory Medicine, Cumming School of Medicine, University of Calgary, Canada
[c] ICF International, Inc., Rockville, MD 20878, USA
[d] The American Society for Clinical Pathology Institute for Science, Technology, and Policy, Washington, DC 20005, USA
[e] Mayo Clinic, Jacksonville, FL 32224, USA

HIGHLIGHTS

- Survey to assess processing protocols of gynecologic surgical pathology specimens
- Majority of pathology labs perform SEE-Fim on risk-reducing specimens.
- Most labs perform SEE-Fim on benign specimens if first sections are suspicious.
- Results suggest detailed processing of fallopian tubes pathology specimens.

ARTICLE INFO

Article history:
Received 20 December 2017
Received in revised form 12 January 2018
Accepted 15 January 2018

Keywords:
Gynecologic tissue
Ovarian/tubal cancer
STICs
SEE-Fim
Biobank
Serous carcinoma

ABSTRACT

Objective. Many high-grade serous carcinomas initiate in fallopian tubes as serous tubal intraepithelial carcinoma (STIC), a microscopic lesion identified with specimen processing according to the Sectioning and Extensive Examination of the Fimbria protocol (SEE-Fim). Given that the tubal origin of these cancers was recently recognized, we conducted a survey of pathology practices to assess processing protocols that are applied to gynecologic surgical pathology specimens in clinical contexts in which finding STIC might have different implications.

Methods. We distributed a survey electronically to the American Society for Clinical Pathology list-serve to determine practice patterns and compared results between practice types by chi-square ($\chi 2$) tests for categorical variables. Free text comments were qualitatively reviewed.

Results. Survey responses were received from 159 laboratories (72 academic, 87 non-academic), which reported diverse specimen volumes and percentage of gynecologic samples. Overall, 74.1% of laboratories reported performing SEE-Fim for risk-reducing surgical specimens (82.5% academic versus 65.7% non-academic, $p < 0.05$). In specimens from surgery for benign indications in which initial microscopic sections showed an unanticipated suspicious finding, 75.9% of laboratories reported using SEE-Fim to process the remainder of the specimen (94.8% academic versus 76.4% non-academic, $p < 0.01$), and 84.6% submitted the entire fimbriae.

Conclusions. Changes in the theories of pathogenesis of high-grade serous carcinoma have led to implementation of pathology specimen processing protocols that include detailed analysis of the fallopian tubes. These results have implications for interpreting trends in cancer incidence data and considering the feasibility of developing a bank of gynecologic tissues containing STIC or early cancer precursors.

Published by Elsevier Inc.

1. Introduction

Historically, most pelvic high-grade serous carcinomas (HGSCs) were classified as ovarian primary tumors, despite the lack of a defined HGSC precursor in the ovary. Subsequently, increased performance of *BRCA1/2* mutation testing and risk reducing surgery (RRS) enabled pathologists to examine adnexal specimens from high-risk

* Corresponding author at: National Cancer Institute, 9609 Medical Center Drive, Bethesda, MD 20892, USA.
E-mail address: goli.samimi@nih.gov (G. Samimi).

https://doi.org/10.1016/j.ygyno.2018.01.016
0090-8258/Published by Elsevier Inc.

women, which resulted in detection of a putative early malignant lesion in the distal fallopian tube, termed serous tubal intraepithelial carcinoma (STIC). Accumulating evidence from histopathologic studies, molecular analyses and preclinical models have strengthened the view that many HGSCs begin as STIC and spread to the ovary and other sites secondarily [1]; however, the frequency with which STIC is reported to be present in surgical tissue varies considerably.

STIC has been reported in 3–8% of RRS specimens [2], concurrently with HGSC in 13%–68% of cases (mean = 37% [95% CI 27%–48%]) and in <1% of specimens removed for benign indications [2–8]. Although the biologic relationship of STIC to HGSC remains undefined [9], detection of STIC is considered clinically important [10]. Specifically, diagnosis of occult STIC may suggest the need for further staging, post-operative surveillance and genetic testing. In cases of symptomatic HGSC, diagnosis of STIC may affect primary site assignment and staging.

Prior to the description of STIC, pathologists typically evaluated grossly unremarkable fallopian tubes sparingly, mostly to document their removal. However, as recognition of STIC increased, experts began advocating for systematic sampling of the fallopian tube for microscopic diagnosis [11–13]. The Sectioning and Extensive Examination of the Fimbria protocol (SEE-Fim) was developed to optimize pathology processing of the fallopian tube [12] and criteria for the diagnosis of STIC were proposed, including p53 and Ki-67 staining [4]. Nonetheless, interobserver agreement among pathologists on the diagnosis of STIC remains variable, and a gold standard for assessing diagnostic accuracy is needed [4,14]. Given that STICs are asymptomatic microscopic lesions, diagnosis is highly dependent upon the extent of processing for microscopic examination [15]. However, little is known about how gynecologic specimens are processed in the U.S., especially with regard to sampling of the fallopian tube and application of the SEE-Fim protocol. The dramatic increase in the reported incidence rate of early stage tubal carcinoma suggests that pathology processing protocols are changing and the large increases in reported rates of late stage tubal cancer suggest that pathologists are increasingly classifying HGSC as tubal primary cancer [16,17]. Further, increased performance of salpingectomy in the U.S. may also be contributing to increasing incidence rates of tubal cancers [18].

Accordingly, we conducted a survey of pathology practices largely in the U.S. to assess methods of routine, diagnostic processing of different types of gynecologic surgical pathology specimens.

2. Materials and methods

2.1. Survey participants

The majority of respondents were recruited through an email distributed to 20,535 usable email addresses listed in the American Society for Clinical Pathology (ASCP) list-serve. This list-serve consists of ASCP members and customers (non-ASCP members), of which 18,348 email addresses are associated with pathology laboratories (hospitals, independent reference laboratories, physician office laboratories, and pathology group practices). The majority of the list-serve members are physicians (56.3%) or technologists (39.3%), with 16.4% also serving as staff pathologists and 9.8% also serving as Laboratory Medical Director or Assistant Director. List-serve members included hospital staff (36.6%) and members of independent reference laboratories (8.1%). Other recruitment methods included distribution to the National Cancer Institute (NCI) Community Oncology Research Program (NCORP), through a network of site coordinators and cold calls to NCORP hospitals. Respondents were asked to provide answers for their entire laboratory, and they had the option to submit the survey via the online Google survey, fax, or email.

2.2. Survey instrument

The survey to assess the feasibility of establishing a gynecologic specimen bank for research was developed by the authors (GS, MES, MAD, BT), and was carried out using the Google Survey platform (https://goo.gl/forms/CKiGG7aJczSbclw03). The gynecologic tissue bank survey assessed the practice setting of the laboratory, the volume of surgical pathology specimens processed, including the approximate annual volume, the percentage of gynecologic specimens, and the number of RRS specimens from women at high risk for gynecologic disease or cancer (Fig. 1). The survey also included questions about whether the laboratory has a gynecologic pathology sub-specialty sign-out. These queries provided context for responses to questions related to pathology processing of gynecologic surgical specimens removed for different clinical indications. The full survey is presented in the Appendix.

2.3. Statistical analysis

Survey responses are presented as raw frequencies and percentages for different sampling protocols by indication and practice setting. Respondents who reported receiving RRS specimens were asked to estimate how many specimens they processed annually, which was converted to a categorical variable: <10 specimens, 10–20 specimens, >20–50 specimens, and >50 specimens. Respondents provided 41 free text comments which were summarized. Results were compared by chi-square ($\chi 2$) tests for categorical variables using Stata/IC version 14 (StataCorp, College Station, TX, USA).

3. Results

3.1. Pathology practices

We received 159 survey responses; 72 (45.3%) from academic practices and 87 (54.7%) from non-academic practices (private hospitals, laboratories affiliated with managed health organizations, or private laboratories) (Fig. 1). Pathology laboratories from academic practices were more likely than those from other practice types to report higher annual volumes of surgical pathology specimens and higher percentages of gynecologic specimens (Table 1). The majority of academic practices reported annual surgical pathology specimen volumes of 10,000–50,000 (65.3%), whereas the most frequent volumes among non-academic practices were <10,000 (44.8%). Across practice types, most laboratories reported that 10%–20% of surgical pathology specimens were from gynecologic organs (Fig. 1); this category included a higher percentage of academic practices than non-academic practices (61.1% vs. 43.7%) (Table 1).

Laboratories from academic practices were significantly more likely than non-academic practices to report having a gynecologic pathology sub-specialty sign-out [$\chi 2$ (degrees of freedom (df) = 2, N = 157) = 30.96, $p < 0.001$]. Although RRS specimens were handled by 102 of 159 of practices (72.3%), these cases were more common in academic practices (87.5%) vs. non-academic settings (59.8%). Laboratories reported estimated annual numbers of RRS specimens ranging from 1 to >50. Laboratories from academic practices were somewhat more likely to report higher estimated annual numbers of RRS specimens than non-academic practice types.

3.2. Processing gynecologic tissue

Laboratories were asked about how their laboratories processed gynecologic specimens in different clinical contexts (Fig. 2 and Table 2). Overall, 74.1% of laboratories reported using SEE-Fim to process RRS specimens and 56.9% reported using SEE-Fim to process HGSC (stages I, II, IIIAi) (Fig. 2). In the context of surgery for benign indications, final specimen processing was related to microscopic findings in the initial sections submitted; when first sections demonstrated STIC, epithelial