



Gynecologic cancer surveillance in the era of SARS-CoV-2 (COVID-19)

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ABSTRACT

The SARS-CoV-2 (COVID-19) pandemic has significantly impacted the management of patients with gynecologic cancers. Many centers have reduced access to routine visits to avoid crowded waiting areas and specially to reduce the infection risk for oncologic patients. The goal of this review is to propose a surveillance algorithm for patients with gynecologic cancers during the COVID-19 pandemic based on existing evidence and established guidelines. It is time to consider strategies based on telemedicine and to adapt protocols in this new era. We hereby propose a strategy for routine surveillance both during and beyond the pandemic.

INTRODUCTION

The SARS-CoV-2 (COVID-19) pandemic has impacted the standard of healthcare worldwide and the treatment of cancer patients. Some gynecologic cancer societies have shared their strategies to treat gynecologic cancer patients during this time, providing options to decrease the risk of transmission and simultaneously reducing the pressure on health systems.¹⁻⁴ As efforts to contain the spread of COVID-19 are starting to show declines in the number of positive cases in many regions, it is time to question how healthcare systems are going to address the post-pandemic care of patients with gynecologic cancers. One of the most important challenges is how to restart routine clinical activity where the infection risk is still present and restrictions on hospital visits are necessary. Cancer patients are a vulnerable group at risk of COVID-19 infection, and when infected may suffer more deteriorating conditions and poorer outcomes.⁵⁻⁷ In the COVID-19 scenario, the potential threat of infection to cancer survivors should be considered.

In this context, to reconsider how we are delivering healthcare is a priority. The COVID-19 crisis could be a catalyst for integrating telemedicine into healthcare systems, reducing in-person consultations, and minimizing patient and health worker exposure.⁸⁻¹¹ On the one hand, telemedicine provides access to remote care, minimizing the risk of exposure to infection, allowing adaptations to healthcare delivery, and increasing acceptance and adherence to care plans by patients. Telemedicine also avoids unnecessary hospital visits that are a potential waste of time and resources, as well as contributing to air pollution.¹²⁻¹⁴

Conversely, there is an important concern with telemedicine regarding privacy and also the element of dehumanizing clinical care. Providers have to promote safe and compassionate delivery of care through telemedicine. Recommendations enabling practitioners to reinforce empathy and enhance patient satisfaction during consultations have also been published.^{15 16}

In an effort to optimize care of gynecologic cancer survivors during the COVID-19 pandemic era, the multidisciplinary gynecologic cancer team at the Hospital del Mar reconsidered patterns of surveillance in order to propose telemedicine-based follow-up strategies for cervical, endometrial, and ovarian cancer patients. A review of the evidence-based data and established guidelines was performed to identify signs of recurrence and abandon unnecessary or wasteful interventions.¹⁷⁻²⁴ As a consequence, we propose telemedicine-based, risk-stratified surveillance schemes supported by evidence and a shared decision-making program for gynecologic cancer survivors in the COVID-19 era.

Telemedicine-Based Risk-Stratified Surveillance in Gynecologic Cancer Survivors

There is poor evidence to suggest that hospital-based follow-up regimes and standardized imaging protocols impact survival in gynecologic cancer survivors.^{15 25 26} However, such an approach has been part of standard clinical practice. Key barriers to wider adoption of less intensive follow-up regimes include fears and misconceptions from both patients and providers that 'more is better'.²⁷ In the context of risk of infection from COVID-19, the key to implementing change in the traditional surveillance strategy has been developing practitioners' skills, and counseling and educating patients. It is important to highlight that the main objective of surveillance in gynecologic cancer survivors is to detect relapses that could potentially be curable. Avoiding false expectation and a sense of security is essential because in most cases relapses are clinically detectable. Accordingly, education about signs of relapse, as well as treatment-related toxicity, has been critical to optimize care and patient awareness.²¹ In that sense, after treatment completion, it is essential to counsel patients about the aim of surveillance.

Review

One further step in improving patient satisfaction and adapting guidelines has been to elaborate a shared decision-making, telemedicine-based follow-up program. The aim of this program in our hospital was to adapt surveillance to the circumstances surrounding COVID-19 with a special focus on the individual patient and their risk of relapse. Telemedicine is the key element in this new surveillance approach.^{11 27 28} Telemedicine plays a role in evaluating signs of recurrence, as well as the side effects of surgical and systemic treatments. Furthermore, telemedicine is also essential in patients' self-management, allowing them to arrange a face-to-face visit to be seen back in the hospital in case there is any change in their clinical condition.

In designing a surveillance strategy we stratified risk of relapse depending on the site of disease, clinical stage at the time of diagnosis, and other known specific prognostic factors taking into account the following considerations.^{18–20}

1. Most recurrences are diagnosed within 36 months after definitive treatment completion. Therefore, closer face-to-face or telematic follow-up, every 3–4 months in the first 2–3 years, is recommended.^{29–33}
2. Rate of recurrence falls between the third and fifth year, then a less intensive approach every 6–12 months is considered. At this time, a shared decision-making, telemedicine-based follow-up program is offered. Based on their personal preferences, patients are given the option of choosing between two options:
 - Semi-telemedicine follow-up regimen: physical examination follow-up performed every 12 months, alternatively with a telemedicine consultation at 6 months.
 - Open telemedicine consultation. When clinically necessary or in the case of new symptoms, the patient can arrange a face-to-face visit within 3–5 days.
3. After 5 years of surveillance, gynecologic cancer survivors should undergo routine evaluation by a general gynecologist or general practitioner.

After taking into account the above considerations, at the time of completion of initial therapy, patients are offered the option of a combined pre-arranged face-to-face and telemedicine surveillance or open telemedicine surveillance. First, patients are educated about the benefits and tradeoffs of both options in terms of detection of

relapse, oncologic outcomes, expectations, and accessibility to the health system. After considering all aspects and addressing their concerns, patients choose between the two options. Finally, a tailored follow-up program is designed. All members of the multidisciplinary team play an important role in involving patients in surveillance and health education, which also includes psychological support and information on the role of the specialist nurse (case manager nurse). The case manager contact number is provided in order to schedule a face-to-face visit in the event of signs or symptoms suggesting disease relapse. In such cases, a priority face-to-face visit is scheduled with a physical examination and specific tests, if indicated. Ideally imaging and laboratory tests should be scheduled on the same day of the visit.

Telemedicine Risk-Stratified Surveillance by Disease Site

Cervical Cancer

Low Risk (FIGO 2009 stage IA-IB1)

Risk of relapse in patients with early cervical cancer is approximately 6%–15%, with up to 67.5% of cases being symptomatic.^{20 34 35}

Patients who have undergone fertility-sparing treatment remain at risk of tumor recurrence, and the recommendation is that they be followed due to the necessity for closer cervical assessment for lower genital tract dysplasia.^{20 36}

Recommendations

- ▶ A face-to-face visit with physical and pelvic examination alternating with telemedicine evaluation every 3 months performed by a gynecologic oncologist from the multidisciplinary team (figure 1).
- ▶ Cytology and human papillomavirus (HPV) detection are recommended at 12 and 24 months, and then yearly after fertility-sparing surgery.^{35–37}
- ▶ Imaging studies are not routinely recommended but are indicated in women with symptoms.²⁰

High Risk

Up to 30% of patients with locally advanced cervical cancers will relapse after complete response to primary treatment. These patients are usually symptomatic and have extrapelvic sites involved

Year	1				2				Type of follow-up	3		4		5	
	3	6	9	12	15	18	21	24		30	36	42	48	54	60
Department	Gyn								Free Follow-up	Gyn					
Type of Consultation															
Clinical Assessment									Semi-Telematic						
Education															
Physical and Pelvic Examination	x	✓	x	✓	x	✓	x	✓	x	✓	x	✓	x	✓	
PAP and HPV test [#]	x	x	x	✓	x	x	x	✓	x						
Imaging	Only if signs or symptoms suggesting relapse or progression														

Figure 1 Low-risk cervical cancer surveillance in the era of COVID-19. Gyn, gynecologic surgeon oncologist. [#]Patients who have undergone fertility-sparing treatment should have a yearly pap smear (PAP) and human papillomavirus (HPV) test with pelvic examination.

Year	1								2				Type of follow-up	3		4		5	
	3	6	9	12	15	18	21	24	30	36	42	48		54	60				
Month																			
Department	Gyn	RT + Gyn	Gyn	Onc + Gyn	Gyn	RT + Gyn	Gyn	Onc + Gyn	Gyn	RT + Gyn	Gyn	Onc + Gyn	Gyn	RT + Gyn	Gyn	RT + Gyn	Gyn	RT + Gyn	
Type of Consultation	👤	👤	👤	👤	👤	👤	👤	👤	👤	👤	👤	👤	👤	👤	👤	👤	👤	👤	
Clinical Assessment				✓															
Education				✓															
Physical and Pelvic Examination				✓															
PAP and HPV test	x	x	x	✓	x	x	x	✓	x	x	x	✓	x	x	x	✓	x	✓	
Imaging																			
Only if signs or symptoms suggesting relapse or progression																			

Figure 2 High-risk cervical cancer surveillance in the era of COVID-19. Gyn, gynecologic surgeon oncologist; HPV, human papillomavirus; Onc, medical oncologist; PAP, pap smear, only after fertility-sparing surgery; RT, radiation oncologist.

in up to 75% of cases.³⁸ Nevertheless, selected patients with small central pelvic tumors will be considered potentially curable.^{31 33 38}

Recommendations

- ▶ Follow-up in cases of high-risk cervical cancer may be performed through face-to-face visits with physical examination and clinical assessment by gynecologic oncologists together or through telemedicine with one of the oncologists from the multidisciplinary team every 3 months during the first 2 years (figure 2).
- ▶ After that, telemedicine-based follow-up and face-to-face visits with physical examination may be performed in an alternating fashion every 6 months. These visits may be performed by the gynecologic oncologists and either the clinical oncologist or the radiotherapy oncologist from the multidisciplinary team during the first 5 years of follow-up.
- ▶ Neither cervical nor vaginal vault cytology or HPV testing improve the detection of disease recurrence after definitive treatment for locally advanced cervical cancer. However, cervical assessment with cytology and colposcopy is recommended every 6 months in patients who have undergone fertility preservation treatment.^{20 36}
- ▶ Imaging studies are not routinely recommended but are indicated in women with symptoms suggestive of relapse. Chest radiography is recommended, particularly in patients who had received radiotherapy or in patients with symptoms.

Endometrial Cancer

The risk-stratified follow-up scheme has been designed according to the stratified risk of relapse classification of endometrial cancer set out in the European Society for Medical Oncology-European Society of Gynaecological Oncology (ESMO-ESGO) guidelines.¹⁹

Low Risk

Less than 5% of patients with low-risk endometrial cancer will relapse.³⁴ Due to this low incidence of recurrence, physical examination alone may be inefficient during follow-up to detect asymptomatic recurrent disease.^{21 30 39} Therefore, a semi-telemedicine follow-up regimen during the first 2 years of surveillance is recommended.^{19 21} An open telemedicine-based surveillance program may be offered to selected patients at risk of infection or frailty.

Low or Intermediate Risk

Although the risk of recurrence in patients with low or intermediate risk is relatively low (10%–15%), patients are usually offered

vaginal vault brachytherapy following surgery.^{34 40 41} Follow-up in these cases is also aimed at assessing the local side effects of this treatment.

High Risk

This group of patients has a higher risk of recurrence (>20%), and therefore intensive multidisciplinary follow-up is recommended, combining physical examination at the hospital and telemedicine assessment of symptoms concerning relapse or toxicity.^{34 42}

Recommendations

- ▶ Clinical visits with physical examination alternating with telemedicine visits every 6 months is performed by a gynecologic oncologist from the multidisciplinary team in patients with low or intermediate risk. (figures 3 and 4)
- ▶ Telemedicine contacts by either a radiation or medical oncologist to assess the possible side effects of local and systemic treatment is performed alternating with face-to-face visits.
- ▶ Cytology and HPV detection are not recommended.
- ▶ Imaging is recommended only in cases with signs or symptoms suggestive of relapse or progression.^{17 21 22}

Invasive Epithelial Ovarian Cancer

There are no data supporting tailored follow-up strategies according to different histologic subtypes of epithelial ovarian cancer.⁴³ Most cases of epithelial ovarian cancer are diagnosed at advanced stages (III-IV) and require treatment with surgery and chemotherapy.¹⁸ Despite a high initial response, approximately 70% of patients with advanced epithelial ovarian cancer and 15% to 40% of those with early-stage disease will relapse in the first 2 years after treatment.³⁴ Pelvic examination is an essential part of the follow-up strategy because up to 50% of recurrences will occur in the pelvis, although the detection rate has low reproducibility and ranges from 15% to 78%.^{43–46}

The role of tumor markers is uncertain. While CA125 level is often increased up to 5 months before clinical diagnosis of relapse, there are contradictory data regarding its impact on patient survival.^{47 48} However, increased CA125 while on surveillance generally is followed by imaging.⁴⁹ Although HE4 has shown promising accuracy for detecting recurrent ovarian disease, there are no conclusive data determining the role of HE4 in surveillance of ovarian patients.⁵⁰

It is unclear whether early initiation of treatment in patients with asymptomatic relapse improves survival. Therefore, there is

Review

					Type of follow-up#			
Year	1		2			3	4	5
Month	6	12	18	24		30	48	60
Department	Gyn	Gyn (+RT)*	Gyn	Gyn (+RT)*		Gyn	Gyn	Gyn
Type of Consultation					Free Follow-up			
Clinical Assessment	✓				Semi-Telematic	✓		
Education	✓					✓		
Physical and Pelvic Examination	×	✓	×	✓		✓		
PAP and HPV test	×							
Imaging	Only if signs or symptoms suggesting relapse or progression							

Figure 3 Low-risk and low-intermediate-risk endometrial cancer surveillance in the era of COVID-19. *If the patient received radiotherapy adjuvant treatment. #Low-risk cases and low-intermediate-risk selected patients followed-up at primary setting after 2 years of follow-up. Gyn, gynecologic surgeon oncologist; HPV, human papillomavirus; PAP, pap smear; RT, radiation oncologist.

controversy regarding the role that clinic-based intensive follow-up of ovarian cancer patients plays in their oncologic prognosis.^{18,48}

Recommendations

- ▶ A combination of telemedicine with face-to-face clinical visits with physical examination is offered (figure 5).
- ▶ Follow-up is performed every 3 months by the medical oncologist assessing symptoms and CA125 level. Alternatively, a face-to-face visit takes place with the gynecologic oncologist. Follow-up of patients treated by surgery alone will be performed by the gynecologic oncologist alone.
- ▶ Imaging is performed only in cases where there is an abnormal finding on physical examination, an increase of tumor markers, or onset of symptoms suspicious for recurrence.

CONCLUSIONS

The COVID-19 outbreak has been a critical challenge for health systems. However, it may be an opportunity to reconsider how we

are delivering healthcare and serve as a catalyst for changes that might otherwise have taken years to be implemented. Patients with gynecologic cancer or a gynecologic cancer history are vulnerable to COVID-19 infection.⁵⁻⁷ In this group of patients, physical distancing and healthcare system access restrictions are particularly important.

Before the pandemic, follow-up guidelines and recommendations were published for the management of gynecologic cancer survivors.¹⁷⁻²² The COVID-19 crisis may encourage implementation of less intensive and more cost-effective surveillance, and it may be an opportunity for integrating telemedicine and shared decision-making processes into the healthcare system. These changes may permanently transform the follow-up of gynecologic cancer survivors and offer a personalized approach.

On the basis of current data, implementation of telemedicine during follow-up of gynecologic cancers may not only be an option during the pandemic but also in the future.¹¹ Successful

									Type of follow-up								
Year	1				2					3		4		5			
Month	3	6	9	12	15	18	21	24		30	36	42	48	54	60		
Department	RT	Gyn + RT	Onc*	Gyn + Onc*	RT	Gyn + RT	Onc*	Gyn + Onc*		Gyn	Gyn	Gyn	Gyn	Gyn	Gyn		
Type of Consultation									Free Follow-up								
Clinical Assessment	✓								Semi-Telematic	✓							
Education	✓									✓							
Physical and Pelvic Examination	×	✓	×	✓	×	✓	×	✓		×	✓	×	✓	×	✓		
PAP and HPV test	×								×								
Tumor Markers	Only in type 2 tumors with elevated markers at diagnosis																
Imaging	Only if signs or symptoms suggesting relapse or progression																

Figure 4 High-intermediate-risk and high-risk endometrial cancer surveillance in the era of COVID-19. *If the patient received chemotherapy adjuvant treatment, otherwise visits will be performed by the RT. Gyn, gynecologic surgeon oncologist; HPV, human papillomavirus; Onc: medical oncologist; PAP, pap smear; RT, radiation oncologist.

Year	1								Type of follow-up	2				3		4		5	
	3	6	9	12	15	18	21	24		30	36	42	48	54	60				
Month	Onc		Onc + Gyn		Onc		Onc + Gyn		Onc		Onc + Gyn		Onc		Onc + Gyn				
Department	Onc	Onc + Gyn	Onc	Onc + Gyn	Onc	Onc + Gyn	Onc	Onc + Gyn	Onc	Onc + Gyn	Onc	Onc + Gyn	Onc	Onc + Gyn	Onc	Onc + Gyn			
Type of consultation	📱	👩	📱	👩	📱	👩	📱	👩	Free Follow-up	📱	👩	📱	👩	📱	👩	📱	👩		
Clinical Assessment				✓						📱	👩	📱	👩	📱	👩	📱	👩		
Education				✓					Semi-Telematic				✓						
Tumor Markers				✓									✓						
Physical and Pelvic Examination	×	✓	×	✓	×	✓	×	✓		×	✓	×	✓	×	✓	×	✓		
Pap and HPV Testing																			
Imaging	Only if signs or symptoms suggesting relapse or progression																		

Figure 5 Epithelial ovarian cancer surveillance in the era of COVID-19. Surgery-only cases: all visits will be performed by a gynecologic surgeon oncologist. Gyn, gynecologic surgeon oncologist; HPV, human papillomavirus; Onc, medical oncologist; PAP, pap smear.

implementation of telemedicine requires education and active participation of all stakeholders, patients, specialized nurses, physiotherapists, and doctors in the multidisciplinary team.

Finally, continuous evaluation of outcomes, not only in terms of oncologic results but also in terms of implementation, team composition, patient perception, and satisfaction and engagement, will need to be ongoing.

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Review

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