



Update in palliative care in gynecologic oncology

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Purpose of review

This review summarizes research advances in quality of life, symptom management, and end-of-life practices within palliative care that can benefit patients with gynecologic cancers.

Recent findings

Addressing fertility issues, sexual side effects, and possible disease recurrence can promote quality of life in gynecologic cancer survivors. Cannabis can provide some benefit for nausea and neuropathic pain, yet for nonneuropathic pain presentations, it does not appear to provide significant benefit in reducing opioid usage. Lastly, palliative care outcomes, such as reduced aggressive care at the end of life and higher rates of hospice enrollment are augmented by the presence of an outpatient palliative care clinic.

Summary

Ongoing advances in palliative care research hold potential for improvement in systems delivery of palliative care as well as symptom management and psychosocial support.

Keywords

cervical cancer, chemotherapy-induced nausea and vomiting, gynecologic oncology, ovarian cancer, palliative care, symptom management, uterine cancer

INTRODUCTION

This article is meant as an update to ‘Palliative Care in Gynecologic Oncology’, published in 2018 [1]. Although the original article broadly outlined major aspects of palliative care as it pertains to symptom management and serious illness conversations within gynecologic oncology, this article will summarize major research and practice guideline updates with respect to the overlap of these two fields.

QUALITY OF LIFE

The WHO defines quality of life (QOL) as ‘an individual’s perception of their position in life in the context of culture (family and society) and value system in which they live and in relation to their goals, expectations, standards, and concerns’ [2]. In practical terms, palliative care providers will often assess whether patients are achieving good control of physical symptoms, experiencing emotional well-being, integrate and maintain their sense of self with changes to their illness, and fulfill their own personal goals.

Therapy side effects can dramatically impact the QOL of gynecologic cancer patients. In a study examining locally advanced cervical cancer patients after neoadjuvant chemotherapy followed by chemoradiation vs. chemoradiation alone [3], both

groups reported significant impairment to sexual QOL, though most reported improvement in sexual activity and sexual enjoyment over time. Both groups were both worse at 12 months compared with baseline for peripheral neuropathy and menopausal symptoms, which patients identified as ‘one of the most disabling treatment related sequelae’.

Survey data examining the QOL and supportive care needs of cancer survivors demonstrates some issues unique to survivors of gynecologic cancers [4]. Among all cancers, survivors report moderate-to-high scores in overall QOL and moderate scores in the psychological QOL domain. In contrast, women with ovarian cancer had lower QOL scores in the psychological domain, thought to be secondary to advanced disease at the time of diagnosis, undergoing aggressive therapies, and poor overall prognosis [5,6]. The most common psychological and existential concern that survivors identified as a need was the fear of cancer recurrence. This was similar among different types of gynecologic cancers

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Curr Opin Obstet Gynecol 2022, 34:6–9

DOI:10.1097/GCO.0000000000000759

KEY POINTS

- Addressing fertility issues, sexual side effects, and the possibility of recurrence can dramatically improve perceived quality of life in patients with gynecologic cancers.
- Cannabis and cannabinoids have been demonstrated to improve nausea and neuropathic pain but evidence is unclear whether it reduces opioid usage overall.
- The addition of a palliative care outpatient clinic can augment the potential benefits of an inpatient palliative care consult team in reducing aggressive care and promoting advance care planning.

(cervical, uterine, and ovarian) but greater for those younger in age and with a shorter disease-free interval (2–5 years). Similarly, ‘the presence of physical symptoms, fatigue, depression, and impaired physical function are associated with distress and poor QOL’ [6,7].

Women with gynecologic cancers ‘reported wanting information about psychological support significantly more often and scored lower on global QOL and higher on depressive symptoms versus women with breast cancer’ [8]. Those at risk for unmet supportive care needs were more likely to be younger, have more advanced disease and more recent treatment, have poor symptom management, have less social support, and live in more remote locations [9].

QOL interventions during ongoing therapy include fertility counseling, which has been shown to improve QOL and sexual wellbeing [10]. Interventions targeting survivors included nursing-led follow-up care and cognitive behavioral therapy, both of which showed a positive effect on patient-reported QOL [9].

SYMPTOM MANAGEMENT

Several recent studies illustrate avenues by which providers may improve symptom management for their patients. Transdermal granisetron has been demonstrated to be 82% more likely to control chemotherapy-induced nausea and vomiting (CINV) than oral ondansetron in gynecologic cancer survivors undergoing chemoradiation [11[■]]. Similarly, the addition of olanzapine 5 mg to standard oral chemotherapy agents demonstrates a 20% relative increase in improvement in CINV associated with platinum-based chemotherapy regimens; this effect is similar to olanzapine 10 mg but reduces the amount of side effects, such as somnolence [12[■]]. Although these measures are not yet considered standard of care in management of CINV, they

represent possible next line agents for patients refractory to standard antiemetic regimens.

In cases of malignant bleeding in patients with advanced disease, practices may shift toward short courses of radiation, similar to ASTRO guidelines recommending single or short course fractions for bone metastases [13]. Short course radiation therapy addresses symptomatic disease while minimizing patient burden and toxicity compared with conventional long-course regimens [14[■]].

One particular aspect of symptom management deserves special attention. As more and more local, state, and national governments have legalized the medicinal and, at times, recreational use of cannabis products, oncologists may face increasing requests from patients for guidance on the use of cannabis products in managing their symptom and side effect burdens. However, substantial, high-quality research on the efficacy of cannabis products pales in comparison to the level of popular excitement and widespread usage. In 2020, the Society of Gynecologic Oncology released practice guidelines directing the usage of cannabinoids in cancer patients, highlighting their effectiveness in CINV and neuropathic pain [15].

Cannabis and cannabinoids have been demonstrated to be helpful in treatment of chemotherapy-induced nausea and vomiting but evidence is lacking comparing them to newer antiemetic agents [15]. Cannabinoids demonstrate utility in the prevention of neuropathy secondary to taxane therapy (level II). Most commonly, cannabinoids are used for the management of cancer-related pain (level II). Similarly, multiple articles report usage of cannabinoids for anorexia and insomnia in addition to the above symptoms. In a survey of gynecologic cancer patients, most patients felt that it was effective in helping their symptom either when used alone or in conjunction with other medical treatments [16]. The survey noted a decrease in opioid usage with concomitant cannabinoid use [16,17], however, randomized, double-blinded, placebo-controlled trials of THC, THC:CBD, and nabiximols in all cancer patients did not demonstrate a significant reduction in opioid usage following initiation of cannabinoids [18,19]. If the legal environment permits, providers may consider validating patients pursuing cannabis and cannabinoid products for management of CINV and neuropathic pain, yet should temper unrealistic expectations for significant improvement in nonneuropathic pain.

END-OF-LIFE CARE

As patients with incurable disease continues to progress, providers may face the challenge of finding the

ideal time to introduce discussions of palliative and hospice care. Ideally, per American Society of Clinical Oncology (ASCO) guidelines [20], palliative care should be introduced early in the disease course for patients to derive the most benefit. Recent research reveals that the structure and breadth of palliative care services in a health system may impact the utility of palliative care in changing patient trajectories. Although palliative care consultation in general is associated with greater advance care planning documentation, less aggressive care at the end of life, and increased hospice enrollment, gynecologic cancer patients followed in an outpatient palliative care clinic had significantly lower rates of aggressive care (25 vs. 44%) and higher rates of hospice enrollment (92 vs. 82%) than patient seen by an inpatient palliative care team [21]. Although many health systems may only feature an inpatient palliative care consult team, the overall efficacy of such a team in achieving palliative-related outcomes may rely on the creation of an outpatient palliative care clinic to provide continuity of care.

Two recent studies examined the prognostic factors in gynecologic cancer patients that would warrant prompt discussion of end-of-life care planning and possible referral to hospice. A short remission period and frequent hospitalizations/procedures for pleural effusions and ascites may be indicators [22]. Additionally, hypercalcemia has been noted to be a warning sign of a poor prognosis. Furthermore, 'when additional RFs are present (brain mets, >1 site of metastasis, ionized calcium $>=5.9$ mg/dl, and serum corrected calcium $>=12.4$ mg/dl),' this should warrant goals of care discussion regarding further treatment hopes and the possibility of hospice [23]. Patients with hypercalcemia and one, two, or three of these risk factors survived 38 vs. 64 vs. 126 days, respectively. Although other prognostic signs, such as malignant bowel obstruction, are quite variable in terms of the actual quantity of time, electrolyte disturbances, such as hypercalcemia may often be overlooked as a more ominous sign.

CONCLUSION AND FUTURE DIRECTIONS

Further advancements in palliative care will continue to explore the nature of integration of palliative care into complex health systems, particularly with oncology practices, in order to yield the most effective outcomes for patients. Future research into novel therapeutics, including the growing body of research into psychedelic-assisted therapy for patients with advanced cancer, may yield novel therapeutic avenues for challenging symptoms, such as end-of-life anxiety and depression. Finally, further exploration of complex psychosocial interventions for QOL may

open the foundation for promoting resilience and flourishing in cancer survivors.

Acknowledgements

We would like to thank Dr. Gottfried Konecny for his support.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

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Changes to standardized nausea regimens for chemotherapy are of significant importance, and the possible benefit of transdermal granisetron may dramatically change many providers' practices.

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Once again, moving from standard antiemetic regimens to incorporate other agents, such as antipsychotics, may influence many providers' practices.

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