



Contents lists available at ScienceDirect

Gynecologic Oncology

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

Review Article

Locally advanced vulva cancer: A single centre review of anovulvectomy and a systematic review of surgical, chemotherapy and radiotherapy alternatives. Is an international collaborative RCT destined for the “too difficult to do” box?

Rachel Louise O'Donnell ^{a,b,*}, Leen Verleye ^{a,1}, Nithya Ratnavelu ^a, Khadra Galaal ^{a,2}, Ann Fisher ^a, Raj Naik ^a

^a Northern Gynaecological Oncology Centre, Queen Elizabeth Hospital, Gateshead NE9 6SX, UK

^b Northern Institute for Cancer Research, Newcastle University, Medical School, Framlington Place NE2 4AH, UK

HIGHLIGHTS

- There is no consensus for the management of locally advanced vulval cancer.
- Evidence for surgery, chemotherapy, or radiotherapy is inadequate and biased.
- Survival appears most favourable with surgery or chemoradiation ± surgery.
- Data describing treatment related morbidity and quality of life is lacking.
- The basis of an international RCT to determine the best approach is discussed.

ARTICLE INFO

Article history:

Received 18 September 2016

Received in revised form 1 December 2016

Accepted 8 December 2016

Available online xxx

Keywords:

Locally advanced vulval cancer (LAVC)

Anovulvectomy

Colostomy

Chemoradiation

Exenteration

ABSTRACT

Introduction. Treatment of locally advanced vulva cancer (LAVC) remains challenging. Due to the lack of randomised trials many questions regarding the indications for different treatment options and their efficacy remain unanswered.

Methods. In this retrospective study we provide the largest published series of LAVC patients treated with anovulvectomy, reporting oncological outcomes and morbidity. Additionally, a systematic literature review was performed for all treatment options 1946–2015.

Results. In our case series, 57/70 (81%) patients were treated in the primary setting with anovulvectomy and 13 patients underwent anovulvectomy for recurrent disease. The median overall survival (OS) was 69 months (1–336) with disease specific survival of 159 months (1–336). Following anovulvectomy for primary disease, time to progression and OS were significantly higher in node negative disease (10 vs. 96 months; 19 vs. 121 months, $p < 0.0001$). Post-surgical complications were observed in 36 (51.4%), the majority of which were Grade I/II infections. There was one peri-operative death.

Review of the literature showed that chemotherapy, radiotherapy or combination treatments are alternatives to surgery. Evidence relating to all of these consisted mostly of small retrospective series, which varied considerably in terms of patient characteristics and treatment schedules. Significant patient and treatment heterogeneity prevented meta-analysis with significant biases in these studies. It was unclear if survival or morbidity was better in any one group with a lack of data reporting complications, quality of life, and long term follow-up. However, results for chemoradiation are encouraging enough to warrant further investigation.

Conclusions. There remains inadequate evidence to identify an optimal treatment for LAVC. However, there is sufficient evidence to support a trial of anovulvectomy versus chemoradiation. Discussions and consensus would be needed to determine trial criteria including the primary outcome measure. Neoadjuvant chemotherapy or radiotherapy alone may be best reserved for the palliative setting or metastatic disease.

© 2016 Elsevier Inc. All rights reserved.

* Corresponding author at: Northern Gynaecological Oncology Centre, Queen Elizabeth Hospital, Gateshead NE9 6SX, UK

E-mail addresses: Rachel.O'Donnell@newcastle.ac.uk (R.L. O'Donnell), Leen.Verleye@kce.fgov.be (L. Verleye), Nithya.Ratnavelu@ghnt.nhs.uk (N. Ratnavelu), K.Galaal@nhs.net (K. Galaal), Ann.Fisher@ghnt.nhs.uk (A. Fisher), Raj.Naik@ghnt.nhs.uk (R. Naik).

¹ Present address: Belgian Health Care Knowledge Centre (KCE), Doorbuilding, Boulevard du Jardin Botanique 55, Brussels, Belgium.

² Present address: Royal Cornwall Hospital, Truro, Cornwall TR1 3LJ, UK.

Contents

1. Introduction	0
2. Methods	0
2.1. Case series	0
2.2. Systematic literature review	0
3. Results	0
3.1. Case series	0
3.2. Anovulvectomy for primary treatment of LAVC	0
3.3. Anovulvectomy for locally recurrent disease	0
3.4. Morbidity	0
4. Literature review	0
4.1. Radical surgery (n = 12 studies)	0
4.2. Reconstructive surgery	0
4.3. Neoadjuvant radiotherapy (n = 5 studies)	0
4.4. Neoadjuvant chemotherapy (n = 5 studies)	0
4.5. Concurrent chemoradiation with or without subsequent surgery (n = 19 studies)	0
4.6. Concurrent chemoradiation versus surgery (n = 3 studies)	0
4.7. Targeted therapies	0
4.8. Recurrent disease	0
5. Discussion	0
6. Conclusion	0
Contribution to authorship	0
Conflict of interest	0
Details of ethics approval	0
Funding	0
References	0

1. Introduction

Surgery forms the cornerstone of management of vulval cancer. Approximately one third of vulval cancer patients present with locally advanced vulval cancer (LAVC) [1], for which there is little consensus regarding its definition. We have defined LAVC as cancers which encroach upon or cross the borders with surrounding structures such as the urethra or anus. Interest in non-surgical alternative more conservative approaches for this subset of women stems from the recognised psychosexual sequelae and physical morbidity associated with radical surgical resection and in particular, the need for a stoma. There has been little progress made in the last 20 years in the development of guidance for treatment of LAVC and it should be acknowledged that the evidence to date for managing LAVC is entirely based on small phase II trials, uncontrolled studies or retrospective case series without matched controls. It is therefore difficult to group or compare patients owing to the significant heterogeneity in both the patient populations as well as variation in the treatment approach and the complicating factor that many patients treated by primary chemoradiation would have been considered unsuitable for surgery by numerous institutions. Modern medicine dictates the use of evidence-based medicine and in this review we collate the available evidence for surgical management as well as the alternative approaches of chemotherapy, radiotherapy and combination modalities.

In addition, we provide our institute's experience of the surgical management of locally advanced peri-anal tumours treated with anovulvectomy, which comprises the largest series from a single tertiary centre over 36 years and report the oncological outcomes and morbidity. Finally, we discuss the need and feasibility of a clinical trial to address many of the unanswered questions.

2. Methods

2.1. Case series

A retrospective review of women, 1978–2014, with LAVC treated by anovulvectomy at the Northern Gynaecological Oncology Centre, UK

was conducted. Data from operative records, pathology reports, medical records, the MDT database and death certificates were accessed in conjunction with morbidity data from the prospectively collected departmental database.

The staging workup for patients with LAVC is not standardised. In our institute all patients underwent examination under anaesthesia and preoperative imaging (MRI/CT, from 1990) to define extent of local tumour, lymph node status and presence of distant metastatic disease. PET has been introduced in more recent years to evaluate metastatic disease. In primary diagnosed cases, bilateral groin node dissection (BGND) was also performed. The operative procedure is described in Supplementary Box 1 [2]. All vulval biopsies and excision specimens were reported as advised by the Royal College of Pathologists' Standards and datasets for reporting cancers [3]. The new FIGO staging (2009) was retrospectively determined in all cases predating the revised guidelines [4]. Follow-up was to the last date seen in the outpatient clinics, or last contact by patient or GP.

Primary oncological outcomes included time to progression and overall survival (OS). Univariate associations between these endpoints and other variables were examined using Chi² or Fisher's exact test, as appropriate. Secondary outcomes focused upon treatment-related morbidity. Peri-operative and long-term side-effect frequencies were reported. For OS, patients who died at follow-up (any cause) were considered uncensored, whereas patients alive at last follow-up, or lost to follow-up were censored. Univariate analyses for OS and PFS were generated by Kaplan–Meier survival curves and log-rank (Mantel–Cox) tests for statistical significance.

2.2. Systematic literature review

The aim of this systematic review was to assess the evidence for the impact of surgery, radiotherapy, chemotherapy, and combination chemoradiation treatments on survival in patients with histologically proven LAVC. The secondary objective was to assess associated morbidity with each of these treatment modalities including preservation of anus.

Download English Version:

<https://daneshyari.com/en/article/5695578>

Download Persian Version:

<https://daneshyari.com/article/5695578>

[Daneshyari.com](https://daneshyari.com)