

RESEARCH ARTICLE

Hospital-based Study of Endometrial Cancer Survival in Mumbai, India

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Abstract

Background: Endometrial cancer is common in western women, and the rates are very high; however in India, the rates are as low as 4.3 per 100,000 (Delhi). **Objective:** To estimate the survival of endometrial cancer patients based on age, education, family history, tobacco habit, number of pregnancies, clinical extent of disease and treatment received. **Materials and Methods:** The present retrospective study was carried out at the Tata Memorial Hospital (TMH), Mumbai, India, between 1999-2002. 310 cases treated in TMH were considered as eligible entrants for the study. Five-year survival rates were estimated using actuarial and loss-adjusted (LAR) methods. **Results:** The proportions of patients dying above 50 years of age, non-residents and illiterates was higher than their counterparts. 54.8% of patients had some form of treatment before attending TMH. There were only 4.2% tobacco-chewers and only 6.1% had a family history of cancer. There were 25.8% who had 3-5 pregnancies (not living children) and 38.1% did not remember the pregnancy history. The 5-year overall survival rate was 92%. The five-year rates indicated better prognosis for those aged less than 50 years (97%), non-tobacco-chewers (94%), with no family history of cancer (93%), with localized disease (93%) and those treated with surgery either alone or as a combination treatment (95%). **Conclusions:** The present study showed that endometrial cancer patients with localized disease at diagnosis have a good outcome in India. A detailed study will help in understanding the prognostic indicators for survival especially with the newer treatment technologies now available.

Keywords: Endometrial cancer - survival rate - risk-group - Mumbai, India

Asian Pacific J Cancer Prev, 14 (2), 977-980

Introduction

As per the GLOBOCAN estimates there are a nearly 12.7 million new cancer cases and 7.6 million cancer deaths occurred in 2008 worldwide (Ferlay J). In India, there are 0.88 million cancer cases with an incidence rate (ASR) of 105.5 per 100,000 in women. The incidence of endometrial cancer cases are very low in India; the highest being observed in Bangalore (ASR=4.2) and in Delhi (ASR=4.3), while in Mumbai it was 2.8 per 100,000.

Tata Memorial Hospital (TMH), Mumbai is a premier cancer centre for diagnosis and treatment in India. The present study, a retrospective hospital-based study was conducted at TMH. Survival rates among endometrial cancer patients have improved over the years, as a result of earlier diagnosis. The present study attempts to find out the factors that play a role in prognosis of endometrial cancer.

Materials and Methods

Material

The study was conducted at TMH which included cases registered during the year 1998-2002. The eligibility

criteria for inclusion in the study analysis were those who were diagnosed histologically as malignant and who had completed the initial cancer directed treatment. The exclusion criteria was those whose cancer was not proven histologically as primary endometrial cancer and those who did not complete the initial cancer-directed-treatment. Thus the total number of endometrial cancer cases eligible for analysis in the present study was 310.

Methods

A regular follow-up was done periodically for all the cases. Patients who missed their appointments/do not attend for follow-up visits were sent pre-paid post cards enquiring their health status. Follow-up information was updated through hospital visits/letters/telephones/Mumbai Cancer Registry. All Mumbai resident deaths were matched with the Mumbai cancer registry. The cases are followed up periodically. The endpoint of the study was overall survival.

The study group was analyzed by two age-groups as '≤50 years', and '>50 years', by place of residence as 'Mumbai' and 'Non-Mumbai', by education as 'literate' and 'illiterate' groups based on education, tobacco-chewers or not. Treatment was classified into

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two groups; (1) those treated by surgery, either alone or in combination with other treatment, (2) those not treated by surgery but by radiation or chemotherapy.

Statistical methods

The Actuarial survival rate method (AR) was used to calculate survival rates (Berkson, 1950). It was not possible to obtain the cause of death among those who were reported as dead; thus the overall survival has been reported in our study. Due to the losses to follow-up, Loss-Adjusted Survival Rate (LAR) method was applied to obtain the corrected survival rates for various groups (Ganesh, 2005; 2011). This method takes into account the losses in different strata by adjustment to obtain the corrected survival rates. Estimated deaths are obtained by logistic regression method in those with complete follow-up and then subsequently these estimates were applied to those with incomplete follow-up. Thus by applying the LAR method, overall survival rates obtained for each of the categories are reported. Univariate and multivariate analysis was carried out to compute the survival rates and also the prognostic factors. Log-rank test was applied to test the statistical significance between the groups.

Results

Table 1 describes the patient characteristics with regard to age, residence, religion, literacy, life-style habits as

Table 1. Patient Characteristics of Endometrial Cancer Patients Studied at Tata Memorial Hospital

Characteristics	No.	%
Total Cases:	310	-
Age:		
≤ 50 years	117	37.7
> 50 years	193	62.3
Place of Residence:		
Mumbai	104	33.5
Non-Mumbai	206	66.5
Literacy:		
Literate	78	25.2
Illiterate	220	71
Unknown	12	3.9
Risk Group:		
Localised	127	41
Non-Localised	13	4.2
Unknown	170	54.8
Primary Treatment Recd.:		
Surgery (S,S+)	95	30.6
Others (RT/RT+/CT/CT+)	213	68.7
Unknown	9	0.6
Co-morbid conditions:		
Diabetes;		
Yes	69	22.3
No	217	70
Unknown	24	7.7
Hypertension;		
Yes	99	31.9
No	188	60.6
Unknown	23	7.4
Habits:		
Tobacco Chewers	13	4.2
Tobacco Non- Chewers	210	67.7
Unknown	87	28.1
Family History of cancer:		
Yes	19	6.1
No	213	68.7
Unknown	78	25.2
Number of Pregnancies:		
NIL	31	10
1-2	62	20
3-5	80	25.8
6+	19	6.1
Unknown	118	38.1

tobacco- chewing, family history of cancer, co-morbid conditions as history of diabetes, hypertension, number of pregnancies, risk-group defined as ‘localized’, ‘non-localized’ and treatment received.

Age was classified broadly into two categories viz. ‘≤50 years’, and ‘>50 years’. It is seen that 62.3% of patients were >50 years of age, 66.5% were non-Mumbai and 71% were illiterates. 22.3% had diabetic history and 31.9% had hypertension history. Only 4.2% were tobacco-chewers and only 6.1% had a family history of cancer With regard to pregnancy history (not living children), only 10% were ‘never-pregnant’, and 38.1% didn’t remember the number of pregnancies. The loss-adjusted survival rate (LAR) for factors considered are reported in Table 2.

The Overall five-year loss-adjusted survival rate (LAR) for endometrial LAR was 92%. It is seen that patients aged ≥50 years had the best prognosis (97%) and the difference in the outcome by age was statistically significant (p=0.04). The survival rates based on literacy status, although were different but not significant (p=0.45). With regard to the number of pregnancies, the 5-year survival rates was least for those with six or more pregnancies (89%), but the differences were not statistically significant (p=0.15). Non-tobacco chewers had a 9% survival benefit than those who chewed tobacco and the difference was significant (p=0.038). Those who didn’t have a family history of cancer had a 4% survival benefit than those who had family history of cancer (p=0.32). Those who didn’t have a diabetic history had a

Table 2. Survival Rates: Loss-adjusted Survival Rates (LAR) for Endometrial Cancer by Various Factors

Characteristics	No.	LAR (year)			p-value
		1 (%)	3 (%)	5 (%)	
AllCases	310	98	95	93	-
Age					
≤50years	117	98	98	97	0.04
>50years	193	98	93	91	
PlaceofResidence					
Mumbai	104	98	93	93	0.78
Non-Mumbai	206	98	95	93	
NumberofPregnancies					
NIL	31	97	97	94	0.15
1-2	62	98	97	95	
3-5	80	100	99	99	
6+	19	95	89	89	
RiskGroup					
Localised	127	98	94	94	0.07
Non-Localised	13	92	92	84	
Unknown (Treated/Recc)	170	98	94	93	
PrimaryTreatmentrecd					
Surgery(S,S+..)	95	97	96	95	0.26
Others(RT/RT+/CT/CT+)	213	98	94	92	
Co-morbidconditions					
Diabetes					
Yes	69	94	90	86	0.059
No	217	99	95	94	
Hypertension					
Yes	99	95	93	91	0.27
No	188	98	95	93	
Habits					
Tobacco Chewers	13	100	92	85	0.038
Tobacco Non- Chewers	210	99	97	95	
Family History of cancer					
Yes	19	100	95	89	0.32
No	213	98	95	93	

8% survival benefit than those who had diabetes and the difference was not significant ($p=0.06$). Similarly for those with hypertension history, the survival rates was 91% while it was 93% for those who didn't have hypertension history and the difference was not significant ($p=0.27$).

It is seen that survival by clinical extent of disease was poorer for non-localized disease patients. The five-year survival rates was 93% and 85% for localized and non-localized disease respectively. A large number of patients had some treatment before attending TMH but the survival rate was similar to those with localized disease seen at TMH, and the differences were significant ($p=0.07$).

Surgically-treated patients, treated either as a single or in combination with other treatment modalities, showed a 95% five-year survival, compared to those who were treated with other modalities of treatment like radiotherapy or chemotherapy or in combination (91%) but the difference in rates was not statistically significant ($p=0.26$).

Discussion

Estimation of survival rate is of primary importance since it will indicate the effect of new treatment, if any, compared, to standard treatment. There are not many cancer survival reports from India, mainly because of poor patient follow-up and incompleteness in death registration system. Although there are methods to improve the follow-up response, it is difficult to obtain 100% follow-up and thus the limitations to undertake survival studies. Also the standard methods available in the literature for calculating survival rates are based on 'certain assumptions'. Violation of these assumptions will only result in biased estimation of survival rates by direct application of standard methods, like the actuarial method and thus the method suggested by Ganesh (1995) has been applied to calculate the survival rates, which corrects for the losses to follow-up.

The present study is a hospital-based follow-up study of histologically confirmed endometrial cancer patients, seen at TMH between the years 1999-2002. The total patients eligible for study was 310 cases. An attempt has been made to study the factors, demographic and clinical, that influence the survival. The loss-adjusted rates (LAR) reported are adjusted for losses to follow-up.

The 5-year overall survival (OS) rate for the entire population was 77% (stages I-IV) (Bertelsen et al., 2011) in another study. To investigate how changes in therapeutic strategies during a 30-year period are reflected in survival changes through careful characterization of a population-based series of 1077 endometrial carcinoma patients from Hordaland County, Norway, was undertaken (Trovik et al., 2012). In concordance with increase in endometrial cancer nationally, the number of patients treated from Hordaland County rose from 286 (1981-1990) through 307 (1991-2000) to 484 (2001-2010). Main treatment changes included increase in adjuvant chemotherapy from 0% through 3-9% and a dramatic reduction in adjuvant radiotherapy from 75% through 48-12% (all $p<0.001$). 5-year disease-specific survival increased significantly during this 30-year period, from 75.8 through 80.2-86.9% ($p=0.002$) and overall survival from 67.8 through 71.7 to

77.8% ($p=0.03$) (Trovik et al., 2012). In the present study, the 5-year OS was 92% which was better than both the studies reported here.

Age is known to be an important factor that determines the prognosis. In a retrospective review of 263 patients conducted to assess the relationship between selected clinical and pathological factors and disease free survival (DFS) and overall survival (OS) in endometrioid endometrial cancer patients, it was observed that the worse OS was related to younger age at menopause ($HR=0.932$; 95%CI=0.873-0.996; $p=0.039$) (Gottwald, 2011). A moderate age gradient was observed, with 5-year relative survival decreasing from 90% in the age group 15-49 years to 75% in the age group 70+ year (Chen, 2012). In the present study, it was found that the five-year survival rates for younger patients (≤ 50 years) was better than the older patients.

A pooled German national dataset including data from 11 cancer registries covering a population of 33 million people. 30,906 patients diagnosed with endometrial cancer in 1997-2006 were analysed (Chen, 2012). In a comprehensive population-based survival analysis, prognosis of endometrial cancer moderately varied by age, and strongly varied by stage. 91% for localized, 51% for regional, and 20% for distant stage (Chen, 2012). Worse overall survival was related to higher staging ($HR=2.053$; 95%CI=1.482-2.845; $p<0.001$), (Gottwald, 2011). As expected those with localized disease had better prognosis than the non-localised disease patients and it was significant in the present study which is in agreement with the studies reported earlier.

A total of 26,967 women were studied in Columbia (Barrena et al., 2011). In a multivariable model, uterine RF strongly influenced survival but nodal disease was a more important negative prognostic factor. Five-year overall survival was 68% [95% confidence interval (CI)], 63-72% for group 1 (node positive/no RF) vs 69% (95%CI, 66-72%) for group 5 (node negative/multiple RF). Five-year survival was lower for node-positive patients with RF (58%; 95%CI, 54-61%) than node-positive patients without RF (68%; 95%CI, 63-72%).

Uterine RF strongly influenced survival both in the presence and absence of nodal metastasis

Over the years, effective treatment has been offered which has translated into better survival rates for endometrial cancer patients. Surgically-treated patients, treated either as a single or in combination with other treatment modalities, showed better five-year survival rates.

Tangjitgamol 2010 reported the 5-year Overall Survival to be 83.4%. In a study to investigate changes in therapeutic strategies during a 30-year period, reflected survival rate changes through careful characterization of a population-based series of 1077 endometrial carcinoma patients from Hordaland County, Norway (Trovik, 2012). Overall survival increased from 67.8 through 71.7-77.8% ($p=0.03$). a change in treatment strategy with reduction in adjuvant radiotherapy and more extensive surgery is demonstrated for the same period was attributed to this change. Overall survival was worse and was related to non-radical surgery ($HR=0.240$; 95%CI=0.091-0.636;

p=0.004) (Gottwald, 2011). The outcome in the present study for surgically treated patients was better than those treated with radiotherapy alone or in combination with chemotherapy

A second neoplasia occurred significantly more frequently in diabetic than in non-diabetic patients with endometrial carcinoma, but long-term survival and other clinical and histological features were the same in the two groups. These results indicate that endometrial adenocarcinoma is not intrinsically different in diabetic patients. More importantly, the two groups had a similar 12-year survival rate (p=0.8742). (Papanas, 2006; Gottwald 2011) reported in diabetes type II a hazard ratio of 2.372 (95%CI=1.260-4.466; p=0.008); the presence of diabetes type II and early menopause were connected with worse prognosis in this study. The results from another study suggest that history of obesity and diabetes may increase risk of mortality after endometrial cancer diagnosis; modification of these characteristics may improve survival after endometrial cancer diagnosis (Chia et al., 2007). In an earlier study Bratos et al. (2002), it was found that 82% for women without hypertension and 72% for women with hypertension in a set of endometrial cancer patients. In the present study, those without hypertension had 5-survival rate of 93% compared to those with hypertension (91%).

The present study findings showed better outcome for those with no family history. In the present study, there was clearly significant difference in survival rates among tobacco-users, the 5-year survival rates being 85% and 94% for tobacco-users and non-users respectively.

A study of 740 nulliparous and 3355 parous endometrial cancer patients diagnosed in Norway during the period 1961-1999, showed that the parous women had significantly (p<0.001) better prognosis than nulliparous women. In analyses adjusted for age at diagnosis, clinical stage, and histological type, the HR for parous versus nulliparous women was 0.68 (95% confidence interval, 0.57-0.82) (Albrektsen, et al., 2009) and also reports were similar in an earlier study (Bratos et al., 2002). Similar observations were found in the present study where nulliparous women had poor prognosis than parous women. The observed beneficial effect of pregnancies may be related to a strong exposure to progesterone during pregnancy. However, it is possible that tumors developing in nulliparous and parous women have different biological features. Further knowledge on this issue may provide valuable information that can be used for individualized treatment.

The above study on endometrial cancer survival, has shown that age at diagnosis, extent of disease, family history, diabetes, hypertension and treatment are important determinants for prognosis.

It can be concluded that the present study showed that younger patients (≤ 50 years), no history of diabetes, hypertension, family history of cancer, non-tobacco user, and those diagnosed with localized-disease, treated with surgery, either alone or in combination had better survival than their respective counterparts. A more detailed clinical study will be helpful in understanding the prognostic indicators for survival especially with the newer treatment

technologies available now.

Acknowledgements

The authors wish to express their gratitude towards the Director, Tata Memorial Centre, Mumbai, India.

References

- Albrektsen G, Heuch I, Wik E, Salvesen HB (2009). Parity and time interval since childbirth influence survival in endometrial cancer patients. *Int J Gynecol Cancer*, **19**, 665-9.
- Barrena Medel NI, Herzog TJ, et al (2011). Comparison of the prognostic significance of uterine factors and nodal status for endometrial cancer. *Am J Obstet Gynecol*, **204**, 248.
- Berkson J, Gage RP (1950). Calculation of survival rates for cancer. *Proc Staff Meet Mayo Clinic*, **25**, 270-86.
- Bertelsen K, Ortoft G, Hansen ES (2011). Survival of danish patients with endometrial cancer in the intermediate-risk group not given postoperative radiotherapy: the Danish endometrial cancer study (DEMCA). *Int J Gynecol Cancer*, **21**, 1191-9.
- Bratos K, Roszak A, Cikowska-Woźniak E, Niecewicz P (2002). Analysis of epidemiologic risk factors for endometrial cancer. *Ginekol Pol*, **73**, 945-50.
- Chen T, Jansen L, Gondos A, et al (2012). Survival of endometrial cancer patients in Germany in the early 21st century: a period analysis by age, histology, and stage. *BMC Cancer*, **12**, 128.
- Chia VM, Newcomb PA, Trentham-Dietz A, Hampton JM (2007). Obesity, diabetes, and other factors in relation to survival after endometrial cancer diagnosis. *Int J Gynecol Cancer*, **17**, 441-6.
- Ferlay J, Shin HR, Bray F, et al (2008). GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010.
- Ganesh B (1995). Effect of lost to follow-up in estimating survival rates. ACTA Universitatis, Ser A, Vol. 440, Tampere, Finland, (Ph.D. Thesis, 1995).
- Ganesh B, Rajaraman S, Aleyamma M, Rengaswamy S, Matti H (2011). Loss adjusted hospital and population based survival of cancer patients. IARC Monograph Eds : Sankaranarayanan R., Swaminathan R., Lucas E. Cancer survival in Africa, Asia, the Caribbean and Central America (SurvCan). IARC Scientific Publications volume 162, ISBN 978-92-832-2162-3, Lyon, International Agency for Research on Cancer, 2011.
- Gottwald L, Chałubińska J, Moszyńska-Zielińska M, et al (2012). Endometrioid endometrial cancer--the prognostic value of selected clinical and pathological parameters. *Ginekol Pol*, **82**, 743-8.
- NCRP (National Cancer Registry Programme). Two-year Report of the Population Based Cancer Registries- 2004-2005. NCRP, Indian Council of Medical Research, Bangalore, 2007.
- Papanas N, Giatromanolaki A, Galazios G, Maltezos E, Sivridis E (2006). Endometrial carcinoma and diabetes revisited. *Eur J Gynaecol Oncol*, **27**, 505-8.
- Tangjitgamol S, Manusirivithaya S, Srijaipracharoen S, et al. Endometrial cancer in Thai women: clinico-pathological presentation and survival. *Asian Pac J Cancer Prev*, **11**, 1267-72.
- Trovik J, Mauland KK, Werner HM, et al (2012). Improved survival related to changes in endometrial cancer treatment, a 30-year population based perspective. *Gynecol Oncol*, **125**, 381-7.