

Parameters Predicting Poor Prognosis in Patients with Malignant Ascites in Yangon General Hospital

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Prognosis for patients with malignant ascites is poor and median survival is only a few months. Treatment of malignant ascites ranges from simple drainage procedures to chemotherapy and debulking surgery. Careful selection of treatment modality by using clinicpathological parameters could improve not only the survival but also the quality of life of the patients. So this hospital-based prospective study aimed to find out the parameters predicting poor prognosis among patients with confirmed malignant ascites admitted to Oncology Department, Yangon General Hospital. This study included 102 patients with malignant ascites. Among them, 19(18.6%) were male patients and 83(81.4%) were female with age ranging from 15 to 73 years (mean age 46.35±12.9 years). Common cancers associated with malignant ascites were ovarian cancer (32.35%), stomach cancer (19.61%) and breast cancer (9.80%). Sixty-four percent of patients presented with stage IV. Common metastatic sites were liver (37.27%), peritoneum (16.67%) and lungs (11.76%) and 28 patients (27.45%) had more than one site of metastasis. Eight patients (7.8%) were in Eastern Cooperative Oncology Group (ECOG) performance status score 1 and 23 patients (22.5%) were in ECOG score 4. The time interval between first diagnosis and development of malignant ascites ranged from 0 to 120 months. Only 33 patients (32.4%) were still alive after 6-month follow-up. High serum urea level was associated with better prognosis (OR =0.19, 95% CI 0.04-0.99), however, primary advanced stage (OR=3.30, 95% CI 1.26-258.62), and high serum creatinine level (OR=9.15, 95% CI 1.71-71.21) significantly worsened the prognosis in patients with malignant ascites.

Keywords: Poor prognosis, Malignant ascites

INTRODUCTION

Many symptoms and syndromes are commonly encountered in patients with cancer. Any symptom can be debilitating and prevent the patient and family from achieving goals that are important to them.¹ Ascites is one of the common symptoms and it is an accumulation of fluid within the peritoneal cavity of the abdomen.² Ten percent of all ascites is caused by malignancy, malignant ascites. Malignant ascites is a sign of peritoneal carcinomatosis, the presence of malignant

cells in the peritoneal cavity. Epithelial malignancies, particularly ovarian, endometrial, breast colon, gastric, and pancreatic carcinomas, cause over 80% of malignant ascites. The remaining 20% are due to malignancies of unknown origin.^{3, 4} Increased portal pressures, direct secretion into the abdomen, or a combination of these two mechanisms contribute to the development of malignant

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ascites.¹ It can lead to many distressing symptoms including abdominal distension, abdominal pain, nausea, vomiting, lower body oedema and breathlessness.⁵ The prognosis for patients who develop malignant ascites is very poor and the median survival time is only a few months, depending on the underlying tumor type and stage.⁶⁻⁹ Average survival in this patient population is about 20 weeks from time of diagnosis.⁹

There are different approaches to the treatment of malignant ascites ranging from symptomatic relief with simple drainage procedures to chemotherapy and debulking surgery aimed at treating the underlying cancer.¹⁰ It is envisaged that quality of life and possibly the survival of patients with malignant ascites may be improved with increasing availability and use of appropriate and potent combination chemotherapy.⁹ Careful selection of treatment modality based on prognostic parameters is important approach in management of patients with malignant ascites.

In developed countries, the prognosis in malignant ascites is significantly determined by the primary cancer type, performance of the patients, presence of liver secondary and serum albumin concentration.¹¹ However, there are very few studies that determine the factors predicting the prognosis of patients with malignant ascites in countries with resource constrained setting. Understanding of these influencing factors may have a great imperative in selecting the rational management in country with limited resource like Myanmar. The aim of this study was to find out the parameters predicting poor prognosis among cancer patients admitted to Medical Oncology Department, Yangon General Hospital (YGH).

MATERIALS AND METHODS

This hospital-based prospective study was conducted among cancer patients with malignant ascites, taking treatment at Medical Oncology Department, YGH from July 2016 to June 2017. Malignant ascites

was diagnosed cytologically or if the patients had not undergone laboratory test, the diagnosis must be clinically (history of cancer plus repeated reaccumulation ascites) and/or radiologically confirmed. Patients younger than 21 years and those with non-malignant ascites such as cirrhosis of liver, congestive cardiac failure were excluded.

A total of 104 cancer patients with malignant ascites were recruited during study period but only 102 patients could be studied because two patients were lost to follow-up. Written informed consent was taken after explaining about the nature and procedure of the study. Patient's demographic and clinical data were collected in pretested performs and patient's performance status was identified according to Eastern Cooperative Oncology Group (ECOG) Scale¹² (0 - Asymptomatic, normal activity; 1 - Symptomatic, ambulatory, able to carry out activities of daily living; 2 - Symptomatic, in bed less than 50% of the day, occasionally needs nursing care; 3 - Symptomatic, in bed more than 50% of the day, needs nursing care; 4 - Bedridden; may need hospitalization).

The laboratory parameters (total protein, serum albumin, serum bilirubin, serum urea and serum creatinine) were taken within 1 week of diagnosis of malignant ascites, by taking 5 milliliters of patient's venous blood under aseptic condition and sent to Pathology Department, Yangon General Hospital. Follow-up was done by checking their visits at appointed date and 2 monthly phone calls to the patients or their relatives, inquiring and noting whether the patients were still alive and continued their treatment or expired. Working definition for poor prognosis in this study is defined if the patients die within 6-month follow-up.

Statistical analysis

The proportion of malignant ascites and different tumour types were evaluated in frequency and percentage. Multiple logistic regression analysis was used to find out the relationships between survival status

(alive, death) and major clinicopathological predictors (age, gender, common primary tumours, secondary sites and ECOG status, serum protein, albumin, serum bilirubin, urea and creatinine). p value <0.05 was set as statistical significant.

Ethical consideration

The study received approval from Ethics Review Committee of Department of Medical Research.

RESULTS

Among 102 cancer patients with malignant ascites, 19(18.6%) were male patients and 83(81.4%) were female patients. Age was ranging from 15 to 73 years with mean age 46.35±12.9 years. Higher prevalence of malignant ascites was seen in patients younger than 60 years (84.3%) and only 16.7% of the patients were age 60 and above. Better survival was seen in patient group younger than 60 years but it was not statistically significant (OR=1.38, 95% CI=0.38-5.02). Interval between first diagnosis and the development of malignant ascites ranged from 0 month to 120 months.

Nineteen percent of the patients had malignant ascites since they knew the diagnosis and the time interval between diagnosis of primary cancer and malignant ascite is zero month. Maximum interval between primary cancer and malignant ascites i.e 120 months was seen in patient with invasive duct carcinoma of the breast.

Ascites was diagnosed clinically in 98 cases (96.07%) of the study population which was confirmed by imaging and cytology. Minimal ascites was detected by ultrasound in 4 patients with primary malignancy but laparotomy or cytology could not be done for confirmation in our setting due to limited resource. Commonest cause of malignant ascites was ovarian cancer (32.35%) and common cancer types associated with malignant ascites are shown in Table 1.

Performance status of the patients was assessed by Eastern Cooperative Oncology

Group (ECOG) scale. Eight patients (7.8%) were in ECOG score 1, 24 patients (23.5%) were with ECOG score 2, 47 patients (46.1%) and 23 patients (22.5%) had ECOG score 3 and 4, respectively. More than half of the patients (63.7%) presented with stage IV. Common metastatic sites were liver (37.27%), peritoneum (16.67%), lungs (11.76%), bone (8.82%) and pleura (5.88%).

Table 1. Distribution of cancer types among patients with malignant ascites

Type of cancer	No. of cases	%
Ovarian cancer	33	32.35
Stomach cancer	20	19.61
Breast cancer	10	9.80
Cervical cancer	10	9.80
Rectal cancer	7	6.86
Colon cancer	8	7.84
Testicular germ cell tumour	3	2.94
Others	11	10.78
Total	102	100

Table 2. Clinical and laboratory parameters associated with poor prognosis in patients with malignant ascites

	OR	95%CI	p
Age >60 years	1.38	0.37-5.02	0.62
Female	0.85	0.24-2.60	0.71
ECOG 3&4	1.58	0.57-4.40	0.37
Stage 4	3.30	1.26-8.61	0.01
High serum creatinine	9.15	1.17-71.21	0.03
High serum urea	0.19	0.03-0.98	0.04
Low total protein	0.96	0.31-2.95	0.94
Low serum albumin	1.38	0.46-4.16	0.56
High serum bilirubin	2.43	0.67-8.74	0.17

ECOG=Eastern Cooperative Oncology Group

Twenty-eight patients (27.45%) had more than one site of metastasis and among them, 82.15% of the patients were dead during 6 months follow-up. There was a significant correlation between disease stage and poor survival (OR=3.30, 95% CI 1.26-8.62). Serum creatinine level was high in 16 patients (15.5%) and they were significantly associated with poor survival (OR=9.15, 95% CI 1.71-71.21). Patients with high serum urea level were less associated poor survival (OR=0.19, 95% CI 0.04-0.99). Thirty-three (32.4%) patients were still alive until 6 months follow-up. Association of major clinicopathological parameters and survival status is shown in Table 2.

DISCUSSION

Presence of malignant ascites in cancer patients associated with worse quality of life and the prognosis is usually poor.^{9, 6} Very few studies identified parameters predicting poor prognosis in patients with malignant ascites and to our knowledge, this is the first study of such objective in Yangon General Hospital. As there is female preponderance in this study, ovarian tumour was the leading primary tumour associated with malignant ascites, followed by stomach cancer (19.64%) and breast cancer (9.8%). This finding aligned with the result reported by Ayantunde *et al.*¹⁰ Contrary to previous studies,^{10, 11} proportion of under 60 years patients (84.3%) was high in this study which may possibly be due to increase prevalence of malignancy at younger age in our study centre. Time interval between cancer diagnosis and that of malignant ascites in this study was similar to previous prospective study.¹¹

Both cancer and its therapies such as chemotherapeutic agents, targeted therapies and analgesics may lead to renal impairment.¹³ High level of serum urea, creatinine and low serum albumin levels and performance status are recognized as independent prognostic factors in patients with malignant ascites.¹⁰ Our study also showed that patients with high serum creatinine level had significantly lower survival yet finding from this study regarding association of serum urea level with survival was contrary to previous reports i.e. high serum urea level was associated with poor prognosis. Generally, high serum urea level reflects poor liver and renal function.

Apart from it, several things could increase blood urea level like medication including steroid and antibiotics, dehydration, urinary tract infection and stress. We could not find definitive reason in this study but we may assume that patients who still remained liver function to produce urea had less poor prognosis. It was obvious that the lower the stage of the primary tumour the better

the prognosis. Although statistically not significant, prognosis was also worse in patients with higher bilirubin level and in patients with lower total protein level showing that multi-organ dysfunction could increase motility.

Malignant ascites indicates a grave prognosis and the standard treatment should be aimed to relieve symptom with minimal burden to the patient.¹⁴ Understanding the parameters predicting poor prognosis explicit the choice of therapeutic option and subsequently improve patient's quality of life.

One limitation of study is that sometime patient's survival status could only be confirmed by phone call to the patients or their relatives, when patients failed to visit at appointed date Further study should be done to facilitate best practice in management of malignant ascites.

Conclusion

Advanced stage and creatinine level significantly worsen the prognosis in patients with malignant ascites. Major clinico-pathological parameters predicting the prognosis of patients with malignant ascites should always be assessed in individual patient because understanding of these factors has a great imperative in selecting the rational management.

Competing interests

The authors declare that they have no competing interests.

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