Clinics in Surgery

Research Article
Published: 02 Aug, 2019

The Role of Carcinoembryonic Antigen (CEA) Testing in Primary Care - Does It Exist?

Parminder Kaur, Deepasheree Bapu and Mark Cheetham*

Shrewsbury and Telford Hospital NHS Trust, UK

Abstract

Introduction: The role of Carcinoembryonic Antigen (CEA) as a prognostic marker after colorectal cancer resection with a curative intent is well understood. However, CEA is not a sensitive or specific test for the initial diagnosis of colorectal cancer. Despite this, there has been an increase in the use of CEA testing in the primary care setting for patients with no formal diagnosis of cancer.

Aim: Our study aims to determine whether CEA testing within primary care setting is beneficial or justified.

Materials and Methods: A retrospective review of all patients who had a serum CEA test sent to our trust laboratory from the primary care setting was performed. Patient records were then analyzed to determine whether CEA testing triggered a referral to the hospital and resulted in a diagnosis of cancer.

Results: A total of 314 patients had a serum CEA checked by their General practitioners during the study period. 79% of the patients had a CEA level checked with no pre-test diagnosis of cancer. A total of 39% PF patients were referred to secondary care with 79% of these patients having a CEA level of less than 5 µg/ml. 12% of patients were not referred to secondary care despite an elevated CEA level of greater than 5 µg/ml. CEA levels were elevated in only 42% of the patients who had a subsequent diagnosis of cancer.

Conclusion: CEA should not be used in the primary care setting as a diagnostic test or to determine whether a referral to the secondary care is indicated.

Keywords: Colorectal Cancer; Carcinoembryonic antigen; Primary Care

OPEN ACCESS

Correspondence:
Parminder Kaur, Shrewsbury and Telford Hospital NHS Trust, Mytton Oak Road, Shrewsbury ST3 8XQ, UK, Tel: 07711951518;
E-mail: parminderkaur@doctors.net.uk

Received Date: *05 Jul 2019*
Accepted Date: *30 Jul 2019*
Published Date: *02 Aug 2019*

Citation:
Kaur P, Bapu D, Cheetham M. The Role of Carcinoembryonic Antigen (CEA) Testing in Primary Care - Does It Exist?. Clin Surg. 2019; 4: 2536.

Introduction

The incidence of colorectal cancer is increasing across the world and colorectal cancer is one of the most common causes of cancer related death worldwide [1,2]. Early diagnosis of colorectal cancer results in improved patient survival outcomes [3]. Hence, there is an emphasis on early detection and treatment of colorectal cancers.

Carcinoembryonic Antigen (CEA) is a glycoprotein that is produced by columnar and goblet cells in the normal colonic cells as well as colonic cancer cells. Higher level of CEA is secreted by colonic cancer cells [4,5]. Elevated CEA level has been shown to be a vital prognostic marker for colorectal cancer [6]. The role of CEA as a marker of recurrent disease, after curative colorectal cancer resection is well established. Regular CEA monitoring has been shown to result in earlier diagnosis of recurrences [7-9] and an increase in the treatment of recurrent disease with curative intent [10].

There has been a lot of interest in the role of CEA in the pre-operative period. Wang et al reported an elevated pre-operative CEA level correlated with adverse prognostic indicators like depth of tumor invasion, lymph node metastasis and a post-operative recurrence [11]. Increased pre-operative CEA levels were also shown to be associated with a reduced 5 year survival rate in patients with stage II and III disease [12].

However, there is no role for CEA to be used as a screening test in the general population for the detection of colorectal cancer as it lacks both sensitivity and specificity as a screening tool for colorectal cancer [13,14]. It can be stipulated that measurement of CEA levels should only be performed in the secondary care setting for patients with a known diagnosis of colorectal cancer.

However, over the last few years CEA has been increasingly used in the primary care setting,

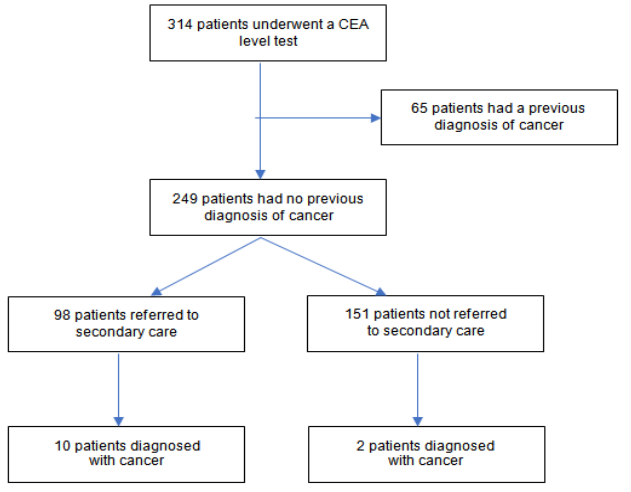

Figure 1: Flowchart showing outcomes of patients undergoing CEA testing.

often as a screening tool, before patients are referred for further investigation. This in turn can lead to an increase in the demand placed on the already overstretched colorectal outpatient clinics and possible mismanagement of those with significant symptoms but a normal CEA level.

The aim of this study was to evaluate the benefit of CEA testing within the primary care setting.

Materials and Methods

This retrospective review was carried out in a high-volume colorectal cancer unit over a six-month period. The electronic records of all patients who had a serum CEA test sent to the trust laboratory from a primary care setting were reviewed. Data regarding patient demographics and CEA levels was collected. Three reviewers then analyzed the trusts electronic records to determine the proportion of these patients referred to secondary care setting and whether a diagnosis of colorectal or other cancers was made within a 6-month period of the CEA being performed. A CEA level of greater than 5 µg/ml was taken to be elevated.

Statistical analysis was carried out by using SPSS software version 17. Continuous variables were expressed as a median with an inter quartile range. Mann Whitney U and Chi Squared tests were carried out to determine statistical significance with a P value of less than 0.05 being considered statistically significant.

Results

314 patients had a serum CEA checked via the primary care setting in the study period. 134 (43%) patients were male and the median age of patients tested was 68 years (range 55 to 78).

65 (21%) of the patients undergoing a CEA level had a pre-existing diagnosis of cancer. Of these, 35 (11%) patients were known to have colorectal cancer and were undergoing active follow up within the Trust. This subset of 65 patients was therefore excluded from our study (Figure 1).

Referrals

Amongst 249 patients, 98 (39%) were referred to secondary care following the result of their CEA test. The remaining 151 (61%) patients remained under primary care.

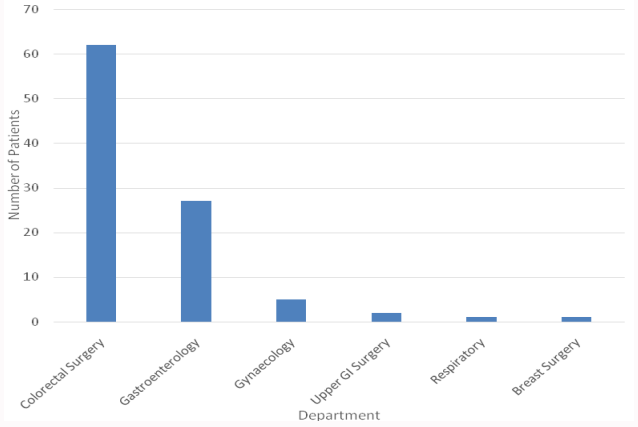

Chart 1: Referral Destinations of Patients Undergoing CEA Testing.

Majority of the referrals to the secondary care was to the colorectal and gastroenterology departments (63% and 28% respectively). The remaining 9% of patients were referred to other specialties (Chart 1).

Median CEA in those referred to secondary care was 3 µg/ml (IQR 1.6 to 4.7) compared to 2.2 µg/ml (IQR 1.3 to 3.25) in those patients who were not referred to secondary care (p = 0.005) (Chart 2).

79% of patients referred to secondary care had a CEA level of less of less than 5 µg/ml. Amongst the patients who were not referred to secondary care, 12% of patients had a CEA level greater than 5 µg/ml compared to 21% in those who were referred to secondary care (p=0.43).

Cancer Diagnosis

A total of 12 (5%) patients had a new diagnosis of cancer during our study period. Out of these, 10 patients were in the group referred to secondary care and 2 patients were in the group who had remained within the primary care setting after their CEA test.

CEA levels were elevated (>5 µg/ml) in 42% of the patients who were diagnosed with cancer.

There were 8 patients diagnosed with colorectal cancers [median CEA 6.25 µg/ml (IQR 2.325 to 33.775)] and 4 patients diagnosed with other cancers [median CEA 2.95µg/ml (IQR 2.425 to 17.85)].

Median CEA in those diagnosed with cancer in the total study population was 4.5 µg/ml (IQR 2.35 to 30.075). In comparison, median CEA of patients in whom a diagnosis of cancer was not established was 2.3 µg/ml (IQR 1.3 to 3.7) (p = 0.198).

In the group of patients not know to have a previous cancer diagnosis the positive predictive value, negative predictive value, sensitivity and specificity of a cancer diagnosis when the CEA level was greater than 5 µg/ml was 15%, 97%, 50% and 85.5% respectively.

Discussion

CEA is the most recognized tumor marker for colorectal cancer and its role in the follow up of patients undergoing curative resection for colorectal cancer is well established [15,16]. However, since its discovery in the 1960s, there has been an interest in the role of CEA as a screening tool for colorectal cancer.

CEA is neither a sensitive or specific marker for diagnosis of colorectal cancer and raised levels have been associated with a range

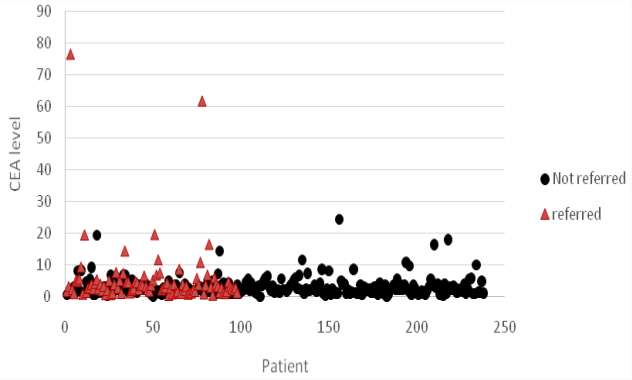

Chart 2: Scatter Graph Showing the Different CEA Levels of Patients. Who Were Referred or Not Referred To Secondary Care.

of other cancers including those of lung, pancreas and stomach and benign conditions such as smoking [17-19].

Our retrospective study adds further evidence to support this position. The median CEA in those diagnosed with cancer from a study population was elevated at 6.25 µg/ml. However, there was no significant difference in the CEA levels between those diagnosed with cancer and those that were not. Furthermore, an elevated CEA level (>5 µg/ml) was found in only 42% of the patients diagnosed with a cancer, which is comparable to the results published in a meta-analysis by Liu et al in 2014 [20].

Despite this, it is clear from our study that CEA levels are still being checked in the primary care setting for diagnostic and screening purposes with 79% of patients (249 of 314 patients) having a CEA level tested despite having no diagnosis of cancer at the time of their initial blood test.

To our knowledge no previous studies have been carried out to assess the referral patterns of those patients undergoing CEA testing in the primary care setting. In our study population, 79% of the patients who were referred to secondary care had a normal CEA level and 12% of patients who not referred to secondary care had an elevated CEA level. Due to the retrospective nature of our study, it was not possible to look at all the referral letters to identify whether other symptomatic and clinical parameters were used to decide which patients were referred to secondary care. However, it is reasonable to assume that CEA levels were not the primary trigger for a secondary care referral and the routine testing of CEA prior to referral is not indicated.

61% of patients who had their CEA levels checked were never referred to secondary care. It is safe to presume these patients had symptoms which concerned primary care physicians sufficiently enough to request a CEA level. However there did not have a definitive test to exclude colorectal cancer. Given CEA's poor sensitivity for detecting colorectal malignancy, 50% in our study, no clinical guidance for it uses in such patients or their additional management depending on their CEA level is available. This is in direct contrast with the use of CA 125 in a primary care setting in patient with suspected ovarian cancer where NICE guidance does exist [21]. As such primary care physicians should be varying of using CEA to rule out colorectal cancer.

There were several limitations to this study. It was retrospective in design and limited by its sample size. Due to the retrospective nature of the study, it was difficult to ascertain pertinent patient information, for example smoking status that could have influenced the CEA levels. Additionally, limited information was available regarding the patient symptoms that initiated the CEA tests and whether these should have led to a secondary care referral despite the result of the CEA test.

Conclusion

This is the first study looking at role of CEA testing in a primary care setting and we conclude that CEA testing in the primary care setting is not indicated in patients with no previous diagnosis of cancer and should not be relied upon to determine their further care. Furthermore we recommend that labs remove CEA from the test panels available to primary care.

References

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015;65(2):87-108.
2. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683-91.
3. Keane MG, Johnson GJ. Early diagnosis improves survival in colorectal cancer. Practitioner. 2012;256(1753):15-8.
4. Gold P, Freedman SO. Demonstration of tumor-specific antigens in human colonic carcinomata by immunological tolerance and absorption techniques. J exp med. 1965;121:439-62.
5. Boucher D, Cournoyer D, Stanners CP, FuksA. Studies on the control of gene expression of the carcinoembryonic antigen family in human tissue. Cancer Res, 1989;49(4):847-52.
6. Veingerl B. Serum carcinoembryonic antigen levels in patients operated for colorectal carcinoma. Wien Klin Wochenschr. 2001;113 Suppl 3:32-8.
7. Duffy MJ. Carcinoembryonic antigen as a marker for colorectal cancer: is it clinically useful? Clin Chem. 2001;47(4):624-30.
8. Fernandes LC, Kim SB, Saad SS, Matos D. Value of carcinoembryonic antigen and cytokeratins for the detection of recurrent disease following curative resection of colorectal cancer. World J Gastroenterology. 2006;12(24):3891-4.
9. Bhatti I, Patel M, Dennison AR, Thomas MW, Garcea G. Utility of postoperative CEA for surveillance of recurrence after resection of primary colorectal cancer. Int J Surg. 2015;16(Pt A):123-8.
10. Primrose JN, Perera R, Gray A, Rose P, Fuller A, Corkhill A, et al. Effect of 3 to 5 years of scheduled CEA and CT follow-up to detect recurrence of colorectal cancer: the FACS randomized clinical trial. JAMA. 2014;311(3):263-70.
11. Wang JY, Lu CY, Chu KS, Ma CJ, Wu DC, Tsai HL, et al. Prognostic significance of pre- and postoperative serum carcinoembryonic antigen levels in patients with colorectal cancer. Eur Surg Res. 2007;39(4):245-50.
12. Su BB, Shi H, and Wan J. Role of serum carcinoembryonic antigen in the detection of colorectal cancer before and after surgical resection. World J Gastroenterology. 2012;18(17):2121-6.
13. Fletcher RH. Carcinoembryonic antigen. Ann Intern Med. 1986;104(1):66-73.
14. Sturgeon C. Practice guidelines for tumor marker use in the clinic. Clin Chem. 2002;48(8):1151-9.
15. Locker GY, Hamilton S, Harris J, Jessup JM, Kemeny N, Macdonald JS, et al. ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. J Clin Oncol. 2006;24(33):5313-27.
16. Verberne CJ, Zhan Z, Van de Heuvel E, Grossmann I, Doombos PM, Havenga K, et al. Intensified follow-up in colorectal cancer patients using

frequent Carcino-Embryonic Antigen (CEA) measurements and CEA-triggered imaging: Results of the randomized "CEAwatch" trial. Eur J Surg Oncol. 2015;41(9):188-96.

17. Alexander JC, Silverman NA, Chretien PB. Effect of age and cigarette smoking on carcinoembryonic antigen levels. JAMA. 1976;235(18):1975-9.

18. Wilson AP, Van Dalen A, Sibley PE, Kasper LA, Durham AP, el Shami AS. Multicentre tumour marker reference range study. Anticancer Res.1999;19(4A):2749-52.

19. Grunnet M, Sorensen JB. Carcinoembryonic antigen (CEA) as tumor marker in lung cancer. Lung Cancer. 2012;76(2):138-43.

20. Liu Z, Zhang Y, Niu Y, Li K, Liu X, Chen H, et al. A systematic review and meta-analysis of diagnostic and prognostic serum biomarkers of colorectal cancer. PLoS One. 2014;9(8):e103910.

21. National Institute for Health and Care Excellence. Ovarian Cancer: recognition and initial management. NICE. 2011. (clinical guideline 122).