
**Usefulness of C-reactive Protein Testing in Assessing Acute Abdominal Pain
in a GP Population**

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Running title: POC CRP testing in Acute abdomen in Primary Care

Abstract:

Introduction:

Various studies conducted in secondary care have evaluated the usefulness of C-reactive protein (CRP) testing in supplementing clinical acumen during a presentation of right iliac fossa (RIF) pain. We aim to assess the effect of point-of-care (POC) CRP testing on admissions to secondary care and the outcome of patients in general practice with RIF pain.

Patients and Methods:

We conducted a retrospective observational study of patients presenting with RIF pain during the period of June 2017 - October 2018. These patients received POC CRP testing and grouped according to levels into 3 tiers: 0-10, 11-50 and >50 mg/L which were then analysed.

Results:

A total of 113 patients were included; [69 men, 44 women], mean age[22.7 ± 12.6] years (range, 6-39years). Women who were pregnant were excluded from this analysis. Clinical evaluation and CRP testing was performed on all patients at presentation.

102patients had CRP level 0-10mg/L. All these patients were managed in primary care and did not require hospital admission. 9patients had CRP levels between 11-50mg/L; 7 from this group were admitted to hospital based on clinical evaluation and CRP levels. 2patients had CRP levels>50mg/L and were admitted to hospital. All 104 patients managed in primary care showed full resolution of symptoms within 5 days. Of the 9 patients admitted to hospital, 7 had appendicitis, and 2 received imaging and discharged within 48 hours or less without further medical intervention.

Conclusions:

POC CRP testing in cases of RIF pain reduced unnecessary admissions from primary care by strengthening clinicians' decision making. Furthermore it has high sensitivity when combined with clinical findings to picking up appendicitis cases. This study highlights the welcome need of such diagnostic aid to help clinicians including allied health professionals in primary care.

Keywords: Primary Care, Point-of-Care C-reactive Protein, Abdominal Pain

Introduction

It is widely agreed that acute abdominal pain, with the inclusion of right iliac fossa (RIF) pain, is a highly common presentation within both acute secondary care [1-2] and primary care [3-4] settings. Accurate clinical assessment is still the most important first step in managing patients who present with an acute abdomen. Studies have demonstrated that this accuracy falls when this is done in the community by GP's by nearly 50% and thus raising the possibility of increasing morbidity and mortality. [5]

To supplement clinical acumen, various laboratory tests including point-of-care (POC) C-reactive protein (CRP) testing have been used in secondary care settings. Within primary care, POC CRP testing is already readily used to inform clinical decisions for conditions such as respiratory tract infections and shown benefit in reducing antibiotic prescriptions and hospital admissions [6-8]. POC CRP has not been evaluated within the community setting to help with management of abdominal pain. CRP is an acute phase protein, where elevated levels are often found in those with infection, inflammation or tissue injury [9]. Various studies have been conducted in secondary care settings, exploring the usefulness of CRP testing in aiding the diagnosis of acute appendicitis[10-13]; but generally no consensus has been established about its accuracy and reliability. More recently; a multicentre study conducted in the United Kingdom (UK), found that 20.6% of patients who underwent an emergency appendectomy for suspected appendicitis had a histological normal appendix [14]. Some even suggest that such negative appendectomies may be more dangerous than the removal of an inflamed appendix [15]. This highlights an important fact in the management of patients who present with RIF pain, in that, they are often needlessly admitted to hospital and procedures then carried out which can raise morbidity and potentially even mortality. GPs act as a gatekeeper to hospitals; which add an extra burden of risk to their decision making. An admission to the emergency department (ED) can cost around four times as much as an appointment with a GP [16-17]. It is postulated that POC testing in addition to clinical acumen in primary care, aims to reduce unnecessary patient admissions to hospital, in order to reduce strain on secondary care services and to reduce unnecessary stress to patients. Our study aims to evaluate the effect of POC CRP testing on admissions to hospital and the outcome of patients in a UK general practice cohort of patients presenting with RIF pain.

Methods:

Design:

This was a evaluation (retrospective observational) study of patients presenting with symptoms of RIF pain at a single general practice surgery during the period of June 2017 to October 2018.

Patient selection:

All patients were clinically assessed as part of their standard care by a GP or Nurse Practitioner. Verbal consent to perform a CRP test was obtained for each patient as part of normal care. Criteria for exclusion included pregnancy, chronic liver disease, major surgery in the preceding month, auto-immune and systemic disorders, renal replacement therapy and other inflammatory diseases.

No ethical approval was required for this study, as this was part of a normal service evaluation program initiated by the Practice.

CRP levels were measured at the POC using the Suresign®Finecare™ point of care analyser (CIGA Healthcare Ltd, Ballymena, UK). The Fine care™ analyser is used for the rapid quantitative measurement of a number of different blood parameters, using Fine care™ disposable Test Cartilages. The Fine care™ Test Cartilage is used to determine the CRP concentration from a small capillary fingerstick blood sample (5-10µL) in approximately three minutes. The basis of the Fine care™ CRP Rapid Quantitative Test is fluorescence immunoassay technology.

The decision of whether or not to admit a patient to hospital was made by the consulting clinician, taking into account of clinical descriptors of peritoneal irritation (low grade pyrexia, rebound tenderness, guarding and rigidity) and CRP levels. Patients were then grouped according to their measured CRP levels: 0-10, 11-50 and >50 mg/L. The clinical outcomes of these patients were then followed up over the next seven days.

Patients that were not admitted to hospital were provided with reassurance and advised to seek medical advice again should they deteriorate. A number of patients were assessed again at the Practice within six hours of being sent home after their first consultation. All patients had their notes retrospectively analysed for seven days post their initial consultation and reviewed against any Emergency Department or Out of Hours communications in the same time period.

Results

A total of 113 patients were included in this analysis. The baseline characteristics are highlighted in Table 1. 69 of these were male and 44 were female. Ages ranged from 6 years to 39 years of age, with a mean age of 22.7 ± 12.6 years. Children aged 6-12 years made up 21 of the males and 9 of the females.

102 (90%) patients had a CRP level between 0-10mg/L. On analysis, clinically only twelve (12) patients exhibited one sign of peritoneal irritation (low grade pyrexia). None were admitted to hospital and symptoms resolved within 5 days of the initial consultation.

9 (8%) patients had a CRP level between 11-50mg/L. 7 of these patients were admitted to hospital. Clinical analysis also correlated with two signs of peritoneal irritation. 6 of these patients had confirmed acute appendicitis at hospital discharge. The remaining patient admitted received further imaging and discharged without further medical intervention within 48 hours of admission (diagnosis Non-specific abdominal Pain). In this patient, symptoms resolved within 5 days of admission. The remaining 2 patients of this group were reviewed at the Practice six hours post-their initial consultation. The same clinician deemed that they did not require admission to hospital as their clinical picture had improved and on follow-up; complete resolution of symptoms were noted within 5 days.

2 (2%) patients had a CRP level above 50mg/L. Both of these patients were admitted to hospital by the clinician concerned. Clinically one patient had signs of peritoneal irritation (rebound and rigidity). This patient had confirmed appendicitis on hospital discharge. The other patient had migration pain but no clinical signs of irritation. On follow-up, she had a diagnosis of inflamed ovarian cyst and was discharged from hospital after further imaging within 48 hours of admission. She recovered completely by Day 5.

General practice remains the main port of help for most patients within the UK health economy. It is well known that General practice like other sectors in the National Health Service (NHS) face ever increasing workload and financial pressures. These pressures have an impact on the workings of the NHS especially when it comes to access to services.

With increasing demand on services and shortage of GPs, primary care is transforming how it works by moving away from the traditional clinical model. More community based practices are now employing paramedics, nurse practitioners or physician associates to provide acute access. These allied health professionals will have varied training backgrounds. For example, the physician associate will have a condensed 2 year post-graduate medical model training compared to the 5 or 6 year undergraduate training that medical students under go before they take on a further 5 years of post-graduate training to become a GP. This is important to recognise as it could lead to different confidence levels in managing certain presenting complaints.

The acute abdomen remains a diagnostic challenge for even the most experienced surgeon. Hence the paramount need for clinicians to consider multiple diagnoses to avoid a mis-diagnosis and subsequent mis-management of a patient. Abdominal pain is a known common presentation not only in ED[18] but also in primary care. A systematic review and meta-analysis looking at the symptom of abdominal pain in general practice showed a high prevalence of abdominal pain presentations in need of immediate investigation and treatment [19]. The study highlighted about 1 in 10 abdominal pain patients suffered from an acute disease such as appendicitis, diverticulitis, or biliary/pancreatic causes.

Clinical assessment remains the pivotal first step in being able to make a diagnosis yet studies [20-22] have found that clinical examination is only accurate in 47-76% and this level of accuracy drops further with junior doctors or those in the community [23]. Furthermore, despite access to medical technology including such as ultrasound, computed tomography (CT), and laparoscopy the misdiagnosis rates of appendicitis have not markedly changed [24].

Studies have already looked at CRP levels in appendicitis cases [25-28]. However, most studies were conducted on patients presenting with suspected appendicitis in the hospital setting with very few studies assessing the diagnostic role of CRP in acute abdomen especially those admitted to a surgical ward with a difficult clinical diagnosis. Two meta-analyses [29-30] over the past 20 years studied the role of CRP in patients with suspected acute appendicitis. Hallan and Asberg[29] reviewed 22 eligible articles including 3436 patients on the accuracy of CRP in patients with suspected appendicitis. Sensitivity and specificity varied considerably from 40–99% and 27–90%, respectively; this was largely due to the use of different cut-off values for a positive test from 5–25 mg/l. They concluded that CRP is a test of medium accuracy and it was not possible to draw firm conclusion on its usefulness [29]. The reason for this conclusion is that only two of the 22 articles examined the question of whether CRP can provide significant independent information in the diagnosis of acute appendicitis and both confirmed this finding. Our study adds to the existing research that CRP levels can be used as a diagnostic aid when combined with clinical evaluation [12-13]. In our small study, the 12 patients in the lowest tertile CRP group who also had clinical signs of peritoneal irritation would have probably been admitted to hospital. The addition of the POC CRP test allowed the clinician to manage the patient conservatively and hence safely with a positive outcome. It ultimately gives the clinician some re-assurance for the forward management of the patient but the evidence from this analysis highlights that if appropriately used POC CRP testing can have the ability to ensure that patients presenting with RIF pain can be managed safely in the right settings of care whether that be in the community or in secondary care where appropriate.

Strengths and Limitations

To our knowledge, this is the first study conducted within UK general practice looking into the usefulness of POC CRP testing as an adjunct in patients presenting with RIF pain. The obtaining of blood samples and CRP measurement were conducted by one named nurse practitioner trained in how to calibrate and operate the POC analyser. This reduced the risk of data error and discrepancy. The results of the CRP test were then interpreted by a qualified GP who would then carry out appropriate management personalised to the patient. Patient safety remained paramount throughout.

Appendicitis cases can present in any age group, but most commonly presents between the ages of 10 and 20 years old [6]. Our patient group studied reflects this cohort. The authors however, do recognise that the sample size in this study is relatively small, thus generalizability is limited. The 2 patients in the 11-50mg/L group who were not admitted to hospital, did not have their

CRP level measured again on their second consultation; thus it is not known whether their CRP levels changed from their initial presentation.

The outcomes of the patients in this study have not been compared with a cohort of similar patients who presented to general practice with RIF pain but did not receive POC CRP testing. This means that we have not been able to statistically quantify any reduction in unnecessary admission rates to hospital with the use of POC CRP testing. This clearly warrants for a similar study to be conducted in general practice to provide evidence of a higher hierarchy and risk-benefit cost analysis.

Conclusion

For primary care clinicians assessing patients presenting with right iliac fossa pain, the use of point of care C-reactive protein testing reduced unnecessary hospital admissions by supplementing the clinician's clinical acumen. Furthermore, point of care C-reactive protein testing has a high sensitivity to when combined with clinical findings to picking up appendicitis cases.

This study highlights the welcome need of such diagnostic aid to help primary care clinicians and warrants further interest into the study of point-of-care testing within primary care.

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Appendices

Table 1 Baseline Characteristics of patients presented between June 2017 and October 2018

Characteristics	n = 113
Demographics:	
Age, mean (± SD)	22.7 (12.6)
Sex M/F (% male)	69/44(61.1)
Factors associated with Functional abdo pain, n (%):	
Belching	12 (10.6)
Flatulence	3 (2.6)
Bloated feeling	9 (7.9)
Dyspepsia	18 (15.9)
Somatization	3 (2.6)
Family history of functional GI complaints	22 (19.5)

Characteristics	n = 113
Red flag symptoms	49 (43.3)
> 2 red flag symptoms	14 (12.3)
Vomiting	2 (1.8)
Wake up at night due to abdominal pain	3 (2.6)
Pain urinating	4 (3.5)
Fever	19 (16.8)
Intra-abdominal comorbidity	1 (0.9)
Abdominal surgery in history	1 (0.9)
Gastroenteritis in previous year	8 (7.1)
Urinary tract infection in previous year	24 (21.2)

Table 2. Outcomes of patients based on CRP tertiles

CRP Level (mg/L)	Number	Admitted to Hospital	Confirmed Appendicitis
0-10	102	0	0
11-50	9	7	6
>50	2	2	1
Total	113	11	7