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1 Background information

Quick info:
The purpose of this care map is to define the appropriate diagnosis and management of acute cholecystitis in adults. The objective is to reduce inappropriate prescribing and referral of patients presenting to any healthcare provider organisation in Qatar. It is intended that the guideline will be used primarily by physicians in both primary/generalist and secondary/specialist care settings.

Scope
Aspects of care covered within this care map include:
• The assessment and management of acute cholecystitis.
• The management of common complications of acute cholecystitis:
  • Acute cholecystitis.
  • Biliary pancreatitis.
Aspects of care not covered within this care map:
• Gallstones in children.
• Non-biliary pancreatitis.
• Common bile duct stones.

Causes of cholecystitis
The most common cause of cholecystitis is gallstones in 90-95% of cases [6].
Other less common causes of acalculous cholecystitis include the following. These causes are also risk factors for the development of calculous cholecystitis [1,7]:
• Dehydration.
• Total parenteral nutrition.
• Cardiovascular disease.
• Diabetes mellitus.
• Sepsis.
• Ischaemia, motility disorders, or direct chemical injury.
• Infections by micro-organism, protozoa, and parasites.
• Collagen disease.
• Allergic reaction.

Complications
Complications of acute cholecystitis include [1,8]:
• Acute cholangitis.
• Biliary pancreatitis.
• Mirizzi's syndrome – extrinsic obstruction of the common hepatic duct by impacted gallstones in the gallbladder or cystic duct.
• Biliary peritonitis.
• Pericholecystic abscess.
• Biliary fistula.
• Perforation of gallbladder.
• Gangrenous gallbladder.
• Sepsis.

Risk factors
Risk factors for acute cholecystitis include [1,6]:
• Female gender.
• Age over 40 years.
• Obesity, including:
  • Obesity treatments.
  • Bariatric surgery.
• Hormonal therapies:
  • Combined oral contraceptive pill.
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- Hormone replacement therapy.
- Repeated pregnancy.
- Haemolytic anaemias.

References:
Please see the care map's Provenance.

2 Definitions

Quick info:

**Acute cholecystitis** is defined as [1]:
- An acute inflammation of the gallbladder, which is often, but not always, attributable to gallstones.

**Acute acalcular cholecystitis** is defined as:
- Acute inflammation of the gallbladder in the absence of evidence of gallstones, or obstruction of the cystic duct [2,3].

**Acute calcular cholecystitis** is defined as [1-3]:
- Acute inflammation of the gallbladder in the presence of gallstones.
- The process typically occurs when gallstones obstruct the cystic duct leading to increased pressure in the gallbladder.
- There are two factors that determine the progression to acute calcular cholecystitis:
  - Degree of obstruction, i.e. partial or complete.
  - Degree of duration, i.e. short or long.
- If the obstruction is partial and of short duration, the patient experiences biliary colic. If the obstruction is complete and of long duration, the patient develops acute cholecystitis.

**Acute cholangitis** is defined as [4]:
- Acute inflammation of the common bile duct or biliary tree.

**Biliary pancreatitis** is defined as [5]:
- Acute inflammation of the pancreas resulting from obstruction of the pancreatic duct by gallstones.

References:
Please see the care map's Provenance.

3 Updates to this care point

Quick info:

Date of publication: 19-Mar-2017
Please see the care map's Provenance for additional information on references, contributors, and the editorial approach.

4 Key recommendations of the care map

Quick info:

The key recommendations of this care map are:

**Diagnosis** (see the 'Investigations' and 'Consider additional imaging and investigations' care points):
- Ultrasound sonography should be performed on every patient presenting with suspected acute cholecystitis [6][L2, RGA2].
- A diagnosis of acute cholecystitis is made when the following are present at the same time [R-GDG]:
  - Thickening of the gallbladder wall by ≥5mm.
  - Ultrasonographic Murphy's sign – inhibited inspiration when the probe is pushed against the right upper quadrant.
  - Pericholecystic fluid.
- An assessment of severity should be made in all patients with acute cholecystitis [6,11]. Use the severity assessment system detailed in the 'Grade III', 'Grade II' and 'Grade I' care points.

**Referral criteria** (see the 'Red Flag' and 'Review response' care points):
- Patients with the following presentations should be referred to the emergency department [R-GDG]:
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- Grade II or III cholecystitis.
- Acute cholecystitis associated with jaundice.
- Suspected acute cholangitis, biliary pancreatitis, or other complication.
- Patients with the following presentations should be referred to be the general surgery outpatient clinic [R-GDG]:
  - Biliary colic.
  - Grade I cholecystitis not responding to medical management.

Medical management (see the 'Medical management' care points):

- Appropriate intravenous fluid administration [11,13].
- Analgesia:
  - NSAIDs such as (intramuscular) diclofenac prevent progression in acute cholecystitis and reduce pain [11][L2].
  - Antimicrobial agents [11,13].

Surgical management options (see the 'Surgical management of acute cholecystitis' care point on the 'Surgical management' pathway page):

- Laparoscopic cholecystectomy:
  - Is recommended in Grade I (mild) cholecystitis [11,14].
  - Surgeons should convert to open cholecystectomy if experiencing difficulty with laparoscopic cholecystectomy, in order to minimise the risk of major complications [14][L2, RGA2].
- Open surgery [14].
- ERCP [9,11,16].
- PTGD:
  - Is recommended in [11,14,17]:
    - Patients with Grade II (moderate) cholecystitis, who do not respond to conservative treatment.
    - Patients with Grade III (severe) cholecystitis.

References:

Please see the care map's Provenance.

5 Abbreviations used in this care map

Quick info:

The abbreviations used in this guideline are as follows:

- **APACHE II**
  Acute Physiology and Chronic Health Evaluation scoring system.
- **CBC**
  Complete blood count.
- **CT**
  Computed tomography scan.
- **ERCP**
  Endoscopic retrograde cholangio-pancreatography.
- **MRCP**
  Magnetic resonance cholangio-pancreatography.
- **NSAIDs**
  Non-steroidal anti-inflammatory drugs.
- **PT-INR**
  Prothrombin time – international normalised ratio.
- **PTGD**
  Percutaneous transhepatic gallbladder drainage.
- **Tc-HIDA**
  Technetium hepatobiliary iminodiacetic acid scan.
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6 Clinical presentation

Quick info:
Features suggestive of acute cholecystitis include [6,9-12]:
• Sudden onset of severe abdominal pain.
• Epigastric or right upper quadrant pain, which radiates to the right shoulder or back.
• Pain that is colicky in nature and lasts from several minutes to hours often occurring at night.
• Nausea.
• Vomiting.
• Pyrexia.
• Prior history of:
  • Biliary disease.
  • Biliary procedure.
  • Placement of biliary stent.

References:
Please see the care map's Provenance.

7 Examination

Quick info:
Examine the abdomen for [1,6,8,12]:
• Tenderness in the right upper quadrant.
• Inspiration, which is inhibited by pain on palpation of the right upper quadrant (Murphy's sign):
  • Murphy's sign has a sensitivity of 50-65% and a specificity of 79-96% for the diagnosis of acute cholecystitis.
  • It is not possible to exclude a diagnosis of acute cholecystitis in the absence of Murphy's sign, due to the low sensitivity.
• A palpable gallbladder.
• Jaundice may indicate Mirizzi's syndrome.

References:
Please see the care map's Provenance.

8 RED FLAG - Refer to emergency

Quick info:
Patients with the following presentations should be referred to the emergency department [R-GDG]:
• Acute cholecystitis associated with jaundice.
• Suspected acute cholangitis, biliary pancreatitis, or other complication.

References:
Please see the care map's Provenance.

9 Perform ultrasonography

Quick info:
Ultrasound sonography should be performed on every patient presenting with suspected acute cholecystitis [6][L2, RGA2].
A diagnosis of acute cholecystitis is made when the following are present at the same time [R-GDG]:
• Thickening of the gallbladder wall by ≥5mm.
• Ultrasonographic Murphy's sign – inhibited inspiration when the probe is pushed against the right upper quadrant.
• Pericholecystic fluid.
Other findings on ultrasound may include [6]:


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- The presence, position, and size of gallstones.
- Gallbladder enlargement.
- Size of the common bile duct.
- Debris echo.
- Gas imaging.

References:
Please see the care map's Provenance.

10 Acute cholangitis

Quick info:
Diagnosis:
- Acute cholangitis is classically indicated by Charcot’s triad of [1,11]:
  - Abdominal pain.
  - Obstructive jaundice.
  - Fever.
- Rigors and a positive history of gallstones or stent placement strongly support the diagnosis [11].

References:
Please see the care map's Provenance.

11 Biliary pancreatitis

Quick info:
The diagnosis of acute pancreatitis is made if at least two of the following are present [18][L2, RGA1]:
- Abdominal pain consistent with acute pancreatitis, i.e.:
  - Upper abdominal pain radiating to the back, which is classically relieved on leaning forwards.
  - Serum amylase ≥3 times the upper limit of normal.
- Characteristic findings on abdominal imaging.
  - All patients with acute pancreatitis should undergo abdominal ultrasound [18][L2, RGA1].

Biliary pancreatitis is typically caused by a stone in the pancreatic duct or at the distal end of the common bile duct, which is causing obstruction to pancreatic outflow [5].

References:
Please see the care map's Provenance.

12 Investigations

Quick info:
Blood tests for acute cholangitis include [11]:
- CBC (for confirmation of an elevated white cell count and the platelet count).
- C-reactive protein.
- Liver function tests.
- Urea and creatinine.
- PT-INR.
- Albumin level.
- Arterial blood gas analysis.
- Blood cultures.

Ultrasound:
- All patients should undergo ultrasound imaging to assess for [11]:


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13 Initial assessment and management

Quick info:
Initial assessment and management:

• Assess haemodynamic status upon presentation and resuscitate as needed [18][L2, RGA1].
• Risk stratify patients according to their risk of mortality using the APACHE II scoring system [R-GDG].
• Consider early intensive care admission for patients with organ failure [18].
• Ensure aggressive rehydration with frequent reassessment of fluid status within the first 6 hours of admission and for up to 48 hours post admission [18][L2, RGA1].
• Routine use of antibiotics is not indicated, unless concomitant acute cholangitis or signs of other extra-pancreatic infection are present [18][L1].
• Enteral nutrition is preferable to parenteral nutrition to prevent infectious complications [18].

References:
Please see the care map's Provenance.

14 Laboratory investigations

Quick info:
There are no specific laboratory blood tests for acute cholecystitis [6,9,11]. The following investigations should be considered [6,11]:

• CBC for leucocytosis.
• Liver function tests.
• C-reactive protein.
• Urea and creatinine.
• Electrolytes.
• Arterial blood gas analysis – can be considered for severe cholecystitis.
• PT-INR, if indicated.
• Serum amylase and lipase.

References:
Please see the care map's Provenance.

15 Management

Quick info:
Initial management comprises of the following [11]:

• IV fluid resuscitation.
• IV antibiotics – according to local protocol and the advice of microbiology.
• ERCP to drain the common bile duct:
  • Endoscopic sphincterotomy should be performed at ERCP.
• Early laparoscopic cholecystectomy (i.e. instead of ERCP) may be considered in patients with mild acute cholangitis.

Further management:
• Following initial management, all patients with confirmed gallstones should undergo:
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• A laparoscopic or open cholecystectomy at 4-6 weeks after ERCP [R-GDG]:
  • 4-6 weeks is necessary to allow the inflammation to subside.
  • As indicated by decrease in the white cell count, bilirubin, and CRP; and resolution of symptoms [R-GDG].

References:
Please see the care map's Provenance.

16 ERCP

Quick info:
Patients with acute pancreatitis and evidence of biliary obstruction from gallstones or concomitant acute cholangitis should undergo urgent ERCP within 24 hours of presentation [18][L2, RGA1].

References:
Please see the care map's Provenance.

17 Consider additional imaging and investigations

Quick info:
Other imaging modalities that may be used to definitively diagnose cholecystitis include [9,6]:
  • MRCP.
  • Tc-HIDA scan.
  • CT scanning:
    • Has added risk of radiation and results are inferior to other tests, such as ultrasound and MRCP.

Consider additional investigations to exclude other differential diagnoses.

References:
Please see the care map's Provenance.

18 Further management

Quick info:
Further management:
  • In patients with confirmed biliary pancreatitis, a laparoscopic cholecystectomy should be performed prior to discharge [18][L2, RGA1].
  • In patients with necrotising biliary acute pancreatitis, laparoscopic cholecystectomy should be performed 4-6 weeks after acute inflammation subsides [18][L2, RGA1].

References:
Please see the care map's Provenance.

19 Differential diagnosis

Quick info:
Differential diagnosis of acute cholecystitis includes the following [1,11]:
Gastrointestinal:
  • Acute pancreatitis.
  • Acute cholangitis.
  • Peptic ulcer disease.
  • Acute hepatitis.
  • Subhepatic appendicitis.
  • Diverticulitis at the hepatic flexure.
  • Crohn's disease.
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• Mesenteric ischaemia.
• Gallbladder malignancy.
• Hepatic abscess.
• Perforated colonic carcinoma.

Urological:
• Ureteric/renal calculi.
• Acute pyelonephritis.

Gynaecological:
• Ectopic pregnancy.
• Fitz-Hugh Curtis syndrome – adhesions between liver and abdominal wall secondary to chronic chlamydia infection.

Other:
• Acute coronary syndrome.
• Right lower lobar pneumonia with pleurisy of the right lung.
• Herpes zoster.

References:
Please see the care map's Provenance.

20 Assess severity

Quick info:
An assessment of severity should be made in all patients with acute cholecystitis [6,11].

References:
Please see the care map's Provenance.

21 Grade III (fulminant or life-threatening) cholecystitis

Quick info:
Grade III (fulminant or life-threatening) cholecystitis [6,11]:
• Dysfunction in any one of the following organs/systems:
  • Cardiovascular dysfunction.
  • Decreased level of consciousness.
  • Respiratory dysfunction.
  • Renal failure.
  • Hepatic dysfunction.
  • Coagulation disorder.

Patients with Grade II or III cholecystitis should be referred to the emergency department [R-GDG].

References:
Please see the care map's Provenance.

22 Grade II (moderate) cholecystitis

Quick info:
Grade II (moderate) cholecystitis [6,11]:
• Absence of organ dysfunction but with a risk of accompanying serious local inflammation.
• Is associated with any of the following conditions:
  • Elevated white blood cell count – >18 x10⁹/L.
  • Palpable tender mass in the right upper quadrant.
  • Persistence of symptoms for >72 hours.

References:
Please see the care map's Provenance.
23 Grade I (mild) cholecystitis

Quick info:
Grade I (mild) cholecystitis [6,11]:
- Absence of organ failure and mild inflammatory changes in the gallbladder.
- Elevated white cell count usually >11 x10⁹/L.

References:
Please see the care map's Provenance.

24 Medical management

Quick info:
Medical management of acute cholecystitis includes [11,13]:
- Appropriate fluid administration.
- Analgesia:
  - NSAIDs such as (intramuscular) diclofenac prevent progression in acute cholecystitis and reduce pain [11][L2].
  - NSAIDs are effective in impacted gallstone disease for prevention of acute cholecystitis [11][L1, RGA2].
- Antimicrobial agents [11,13]:
  - In patients with acute cholecystitis (confirmed by a raised white cell count), start empirical antimicrobial treatment according to local antibiogram and the advice of a microbiologist.

References:
Please see the care map's Provenance.

25 RED FLAG - Refer to emergency

Quick info:
Patients with Grade II or III cholecystitis, should be referred to the emergency department [R-GDG].

26 Review response

Quick info:
Patients with the following presentations should be referred to be the general surgery outpatient clinic [R-GDG]:
- Biliary colic.
- Grade I cholecystitis not responding to medical management.

References:
Please see the care map's Provenance.

27 Medical management

Quick info:
Medical management of acute cholecystitis includes [11,13]:
- Appropriate intravenous fluid administration.
- Analgesia:
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- NSAIDs such as (intramuscular) diclofenac prevent progression in acute cholecystitis and reduce pain [11][L2].
- NSAIDs are effective in impacted gallstone disease for prevention of acute cholecystitis [11][L1, RGA2].
- Antimicrobial agents [11,13]:
  - In patients with acute cholecystitis (confirmed by a raised white cell count), start empirical antimicrobial treatment according to local antibiogram and the advice of a microbiologist.

References:
Please see the care map's Provenance.
Assessment and management of acute cholecystitis

Provenance Certificate

Overview

This guideline document has been developed and issued by the Ministry of Public Health of Qatar (MOPH), through a process which aligns with international best practice in guideline development and localisation. The guideline will be reviewed on a regular basis and updated to incorporate comments and feedback from stakeholders across Qatar.

Whilst the MOPH has sponsored the development of the care map, the MOPH has not influenced the specific recommendations made within it.

This care map was approved on 19 Mar 2017.

For information on changes in the last update, see the information point entitled 'Updates to this care map' on each page of the care map.

Editorial approach

This care map has been developed and issued by the Ministry of Public Health of Qatar (MOPH), through a process which aligns with international best practice in guideline development and localisation. The care map will be reviewed on a regular basis and updated to incorporate comments and feedback from stakeholders across Qatar.

The editorial methodology, used to develop this care map, has involved the following critical steps:

- Extensive literature search for well reputed published evidence relating to the topic.
- Critical appraisal of the literature.
- Development of a draft summary guideline.
- Review of the summary guideline with a Guideline Development Group, comprised of practising physicians and subject matter experts from across provider organisations in Qatar.
- Independent review of the guideline by the Clinical Governance body appointed by the MOPH, from amongst stakeholder organisations across Qatar.

Explicit review of the care map by patient groups was not undertaken.

Whilst the MOPH has sponsored the development of the care map, the MOPH has not influenced the specific recommendations made within it.

Sources of evidence

The professional literature published in the English language has been systematically queried using specially developed, customised, and tested search strings. Search strategies are developed to allow efficient yet comprehensive analysis of relevant publications for a given topic and to maximise retrieval of articles with certain desired characteristics pertinent to a guideline.

For each guideline, all retrieved publications have been individually reviewed by a clinical editor and assessed in terms of quality, utility, and relevance. Preference is given to publications that:

1. Are designed with rigorous scientific methodology.
2. Are published in higher-quality journals (i.e. journals that are read and cited most often within their field).
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3. Address an aspect of specific importance to the guideline in question.

Where included, the ‘goal length of stay’ stated within this guideline is supported by and validated through utilisation analysis of various international health insurance databases. The purpose of database analysis is to confirm the reasonability and clinical appropriateness of the goal, as an achievable benchmark for optimal duration of inpatient admission.

Evidence grading and recommendations

Recommendations made within this guideline are supported by evidence from the medical literature and where possible the most authoritative sources have been used in the development of this guideline. In order to provide insight into the evidence basis for each recommendation, the following evidence hierarchy has been used to grade the level of authoritativeness of the evidence used, where recommendations have been made within this guideline.

Where the recommendations of international guidelines have been adopted, the evidence grading is assigned to the underlying evidence used by the international guideline. Where more than one source has been cited, the evidence grading relates to the highest level of evidence cited:

- **Level 1 (L1):**
  - Meta-analyses.
  - Randomised controlled trials with meta-analysis.
  - Randomised controlled trials.
  - Systematic reviews.

- **Level 2 (L2):**
  - Observational studies, examples include:
    - Cohort studies with statistical adjustment for potential confounders.
    - Cohort studies without adjustment.
    - Case series with historical or literature controls.
    - Uncontrolled case series.
  - Statements in published articles or textbooks.

- **Level 3 (L3):**
  - Expert opinion.
  - Unpublished data, examples include:
    - Large database analyses.
    - Written protocols or outcomes reports from large practices.

In order to give additional insight into the reasoning underlying certain recommendations and the strength of recommendation, the following recommendation grading has been used, where recommendations are made:

- **Recommendation Grade A1 (RGA1):** Evidence demonstrates at least moderate certainty of at least moderate net benefit.
- **Recommendation Grade A2 (RGA2):** Evidence demonstrates a net benefit, but of less than moderate certainty, and may consist of a consensus opinion of experts, case studies, and common standard care.
- **Recommendation Grade B (RGB):** Evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended.
- **Recommendation Grade C1 (RGC1):** Evidence demonstrates a lack of net benefit; additional research is recommended.
- **Recommendation Grade C2 (RGC2):** Evidence demonstrates potential harm that outweighs benefit; additional research is recommended.
- **Recommendation of the GDG (R-GDG):** Recommended best practice on the basis of the clinical experience of the Guideline Development Group members.
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References

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Guideline Development Group members

The following table lists members of the Guideline Development Group (GDG) nominated by their respective organisations and the Clinical Governance Group. The GDG members have reviewed and provided feedback on the draft guideline relating to the topic. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

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Guideline Development Group members

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Responsibilities of healthcare professionals

This care map has been issued by the MOPH to define how care should be provided in Qatar. It is based upon a comprehensive assessment of the evidence as well as its applicability to the national context of Qatar. Healthcare professionals are expected to take this guidance into account when exercising their clinical judgement in the care of patients presenting to them.

The guidance does not override individual professional responsibility to take decisions which are appropriate to the circumstances of the patient concerned. Such decisions should be made in consultation with the patient, their guardians, or carers and should consider the individual risks and benefits of any intervention that is contemplated in the patient’s care.

Acknowledgements

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- Ms Huda Amer Al-Katheeri, Acting Director & Project Executive.
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- Dr Ilham Omer Siddig, Guideline & Standardisation Specialist.
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- Dr Rasmeh Ali Salameh Al Huneiti, Research Training & Education Specialist.
- Mr Mohammad Jaran, Risk Management Coordinator.

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