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REVIEW

Management of septic arthritis and prosthetic joint infection

Lokesh Sharoff[1]

Mark Bowditch[1]

Rhidian Morgan-Jones[1,2]

Author details can be found at the end of this article

Correspondence to:
Lokesh Sharoff; lokesh.sharoff@doctors.org.uk

Abstract

Management of joint infection is an evolving topic. This article reviews the literature on the management of native and prosthetic joint infection and suggests some areas of improvement in short- and long-term management which could lead to better patient outcomes. Surgical management is the mainstay of treatment for native or prosthetic knee infection and aspiration should only be used for diagnostic purposes. A multidisciplinary team approach and compliance with national guidelines, alongside referral networks and pooling of expertise, should be mandatory to improve patient outcomes.

Key words: Antibiotics; Hip; Inflammatory markers; Joint aspiration; Joint washout; Knee; Wound infection

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Introduction

Septic arthritis is a serious and potentially life-threatening condition which causes rapid destruction of the articular cartilage and irreversible damage and arthritis of the involved joint (Geirsson et al, 2007). Prosthetic joint infection is one of the most severe and costly complications following total joint arthroplasty (Aggarwal et al, 2013). Septic arthritis and prosthetic joint infection are significant causes of morbidity, mortality and economic burden associated with increased healthcare costs and prolonged hospital stays.

The incidence of septic arthritis is 2–6/100 000 population (Geirsson et al, 2007). The reported post-arthroscopy infection rate is 0.5–2% and the post-injection infection rate varies from 0.005–0.0002% (Geirsson et al, 2007). This is significant as the number of arthroscopic surgeries has greatly increased in recent years.

The incidence of prosthetic joint infections varies widely, depending on the study population and the definition used. The prevalence of prosthetic joint infection in primary hip and knee replacement procedures is estimated to be between 0.5% and 3% (Cui et al, 2007), and the number of periprosthetic infections is expected to increase as the number of these procedures continues to rise (Kurtz et al, 2005; Pina et al, 2019). The risk of developing septic arthritis increases with the number of risk factors present (Gardner and Weisman, 1990). Patients with rheumatoid arthritis are at particular risk of septic arthritis, associated with high mortality and morbidity (Gardner and Weisman, 1990). The incidence of prosthetic joint infections is also increasing as a result of the ageing population, and the increasing prevalence of comorbidities such as diabetes and obesity (Tande and Patel, 2014). This article reviews the literature on the management of native and prosthetic joint infection and suggests some areas which could improve the short- and long-term management of patients.

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Aetiology

Septic arthritis and prosthetic joint infection can be the result of contiguous or haematogenous spread or iatrogenic causes. Ulcerated skin or penetrating trauma can lead to contiguous spread. Causes of haematogenous spread include urinary tract infection, skin infection or intravenous drug use. Previous intra-articular injection or recent joint surgery can be iatrogenic causes of joint infection.

Risk factors

Risk factors for joint infection include age, inflammatory joint disease, intravenous drug use, immunosuppressive medication, alcohol or drug disorder, diabetes, corticosteroid injection, recent joint surgery, avascular necrosis, joint prostheses, the presence of other infections such as skin infections, and indwelling catheters (Pedersen et al, 2010; Tande and Patel, 2014; Alexiou, 2022; Jeong Bae et al, 2022). An age of over 80 years is associated with an increased risk of infection (Kaandorp et al, 1995).

Pathogenesis

Septic arthritis or prosthetic joint infections can be caused by bacteria, fungi or mycobacteria. The most common causative organisms are *Staphylococcus aureus* and coagulase-negative staphylococci, followed by Gram-negative bacteria and streptococci.

The ability to form biofilms is a key factor in the pathogenesis of prosthetic joint infections (Gbejuade et al, 2015). Biofilms are communities of bacteria that are protected by a matrix of extracellular polymeric substances, making them resistant to antibiotics and host immune responses.

Diagnosis

Diagnosis of septic arthritis or prosthetic joint infections can be challenging, and often requires a combination of clinical, radiological and laboratory investigations (Figure 1). Diagnosis of prosthetic joint infection is difficult as there is no 'gold standard' (Della Valle et al, 2011).

Joint infection is diagnosed by a combination of clinical features, blood and radiological investigations, joint aspiration and results of other tests.

Clinical features

The clinical features of septic arthritis and prosthetic joint infections include pain, swelling, erythema and warmth at the site of the affected joint. However, these symptoms can also be present in other non-infectious inflammatory conditions or with the loosening of an aseptic component. There can be a sinus and/or purulent discharge. Patients can also present acutely and be in septic shock, which requires urgent medical and surgical attention.

Laboratory investigations

Investigations including blood cultures and synovial fluid analysis can help to identify the causative organism and guide specific antibiotic therapy for native joint septic arthritis. Indicators of septic arthritis are purulent discharge or aspirate, synovial fluid white blood cell count >50 000 cells/ul, polymorphonuclear cells >90% and microbial growth from synovial fluid (Ravn et al, 2023).

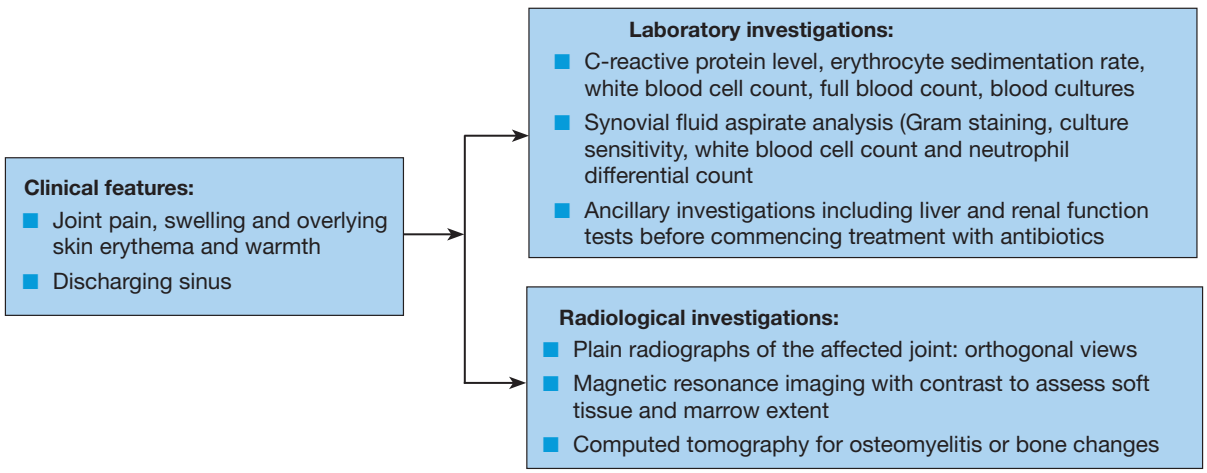

Figure 1. Approach to a patient with septic arthritis or prosthetic joint infection.

Erythrocyte sedimentation rate and C-reactive protein levels can sometimes be normal in joint infections caused by slow-growing organisms and also in immunocompromised patients.

In the subacute setting, a diagnosis of tuberculosis should be kept in mind, especially in patients from endemic areas or who have previously had tuberculosis.

According to the criteria proposed by the Musculoskeletal Infection Society (Parvizi et al, 2011), prosthetic joint infection exists when:

- There is a sinus tract communicating with the prosthesis or
- A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or
- Four of the following six criteria exist:
  1. Elevated serum erythrocyte sedimentation rate and serum C-reactive protein concentration
  2. Elevated synovial white blood cell count
  3. Elevated synovial neutrophil percentage (% polymorphonuclear cells)
  4. Presence of purulence in the affected joint
  5. Isolation of a microorganism in one culture of periprosthetic tissue or fluid
  6. More than five neutrophils per high-power field in five high-power fields observed from histological analysis of periprosthetic tissue at × 400 magnification (Parvizi et al, 2011).

The findings of meta-analyses on the role of inflammatory blood markers in the diagnosis of prosthetic joint infections are summarised in Table 1 (Berbari et al, 2010; Yuan et al, 2015; Shahi and Parvizi, 2016; Huerfano et al, 2017; Xie et al, 2017; Yoon et al, 2018).

Most experts advocate the use of erythrocyte sedimentation rate and blood C-reactive protein levels as markers for assessing patients with a suspected prosthetic joint infection (Spangehl et al, 1999; Patel et al, 2005; Parvizi et al, 2006).

Radiological investigations

Imaging via plain radiographs should be performed for all cases of suspected infection or septic arthritis. This can help identify markers of infection such as soft tissue swelling, periosteal reaction or implants, and is also helpful for follow-up monitoring. In cases of prosthetic joint infection, there may be implant loosening, component malposition or fractures around the implant. Serial plain radiographs may also show progression of loosening or malalignment.

Cross-sectional imaging, such as magnetic resonance imaging, computed tomography and bone scanning, is probably overused in joint infection and has a higher negative predictive value in excluding infections as the specificity is low. They are helpful to look at the integrity of soft tissues and to detect an abscess or osteomyelitis. Table 2 summarises the sensitivity and specificity of imaging in prosthetic joint infection (Signore et al, 2019; Romanò et al, 2020).

Other investigations

Aspiration of joint fluid

This has the highest precision and accuracy for diagnosis of septic arthritis or prosthetic joint infection and will suggest the organism involved. It should always be performed in a sterile environment such as an operating theatre or interventional radiology suite to avoid

Table 1. Result of meta-analyses on the role of inflammatory blood markers in diagnosis of prosthetic joint infections

Test	Sensitivity (%)	Specificity (%)
C-reactive protein	86.9–88.0	73.0–78.6
Erythrocyte sedimentation rate	75–86	70.0–72.3
Interleukin-6	72–97	89–91
D-dimer	89	93
Procalcitonin	53–58	92–95

From Berbari et al (2010); Huerfano et al (2017); Xie et al (2017); Yoon et al (2018)

Table 2. Sensitivity and specificity of imaging in prosthetic joint infection

Type of study	Pooled sensitivity (%) (95% confidence interval)	Pooled specificity (%) (95% confidence interval)
Bone scintigraphy	82 (70–89)	25 (16–36)
Leukocyte scintigraphy	61 (43–76)	77 (63–87)
Combined bone and leukocyte scintigraphy	78 (72–83)	84 (75–90)
Fluorodeoxy-glucose positron emission tomography	96 (88–99)	91 (81–95)
Magnetic resonance imaging	84 (69–92)	60 (38–78)
Radiography	No data	No data
Computed tomography	No data	No data
Combined bone and gallium scintigraphy	No data	No data
Gallium scintigraphy	No data	No data

From Signore et al (2019); Romanò et al (2020)

contamination. The fluid should be collected in sterile pots and blood culture bottles and sent to the laboratory for testing according to locally agreed protocols. Ideally, Gram staining, microbiological culture sensitivity, synovial fluid leucocyte count and neutrophil differential counts should be performed. The concordance between preoperative and intraoperative cultures can vary. If a microbe is in the planktonic stage, this can lead to false-negative preoperative aspiration results. Antibiotics should be stopped at least 2 weeks before aspiration, although if this is not possible in an acute setting, aspiration should ideally be done before starting antibiotics. Patients should remain on broad-spectrum antibiotics until the results of culture and sensitivity are obtained. The most accurate intraoperative culture is obtained from the biofilm behind the implants.

Other tests

Synovial diagnostic assistance tests for substances such as leucocyte esterase, alpha defensin and calprotectin are expensive and not completely diagnostic. They are more helpful to exclude infections. The diagnostic accuracy of the synovial assistance tests complements the measurement of synovial C-reactive protein levels and blood erythrocyte sedimentation rate.

Table 3 lists specific cut-off values that help diagnose prosthetic joint infection. In addition to the tests listed in Table 3, non-gonococcal septic arthritis will typically have white cell counts greater than 100 000/ml and >75% neutrophils (Alexiou, 2022).

Differential diagnoses

The differential diagnoses of joint infection include inflammatory conditions (osteoarthritis, psoriatic arthritis, rheumatoid arthritis and gout), haemarthrosis, trauma, cellulitis, tuberculosis and Lyme disease. Most cases are obvious with a hot swollen joint or a sinus but differentiating between an infected and non-infected joint can be difficult, especially in immunocompromised patients (Alexiou, 2022).

Table 3. Specific cut-off values for diagnosing prosthetic joint infection

Test	Acute prosthetic joint infection <6 weeks	Chronic prosthetic joint infection >6 weeks
C-reactive protein	>100 mg/litre	>10 mg/litre
Synovial white blood cell count	>10 000 cells/µl	>3000 cells /µl
Synovial polymorphonuclear (%)	>90	>80
Erythrocyte sedimentation rate	Not useful	>30 mm/hour

From Trampuz et al (2004); Della Valle et al (2007); Ghanem et al (2008); Zmistowski et al (2014)

Management

The management of septic arthritis or prosthetic joint infection requires a multidisciplinary approach involving orthopaedic surgeons, infectious disease specialists, rheumatologists, microbiologists, tissue viability nurses and physiotherapists. Treatment is complex and often requires a combination of inpatient antibiotic therapy and surgical intervention. The goals of treatment are to eradicate the infection, preserve joint function and minimise the risk of recurrent infection (Figure 2).

Therapeutic aspiration

This is controversial and the authors do not completely agree that therapeutic aspiration is beneficial. Coakley et al (2006) suggested aspirating the joint to dryness as often as necessary, but the authors believe that this should be done only for aseptic inflammatory joints and not for septic joints. Alexiou (2022) suggested aspiration of the septic joint to preserve life, avoid progression to systemic infection, preserve joint function and prevent morbidity associated with complications such as amputation and arthrodesis. However, the authors believe therapeutic aspiration will not help to prevent systemic complications. Aspiration should be used as a diagnostic not a therapeutic tool.

An orthopaedic review should be undertaken shortly after admission as part of a multidisciplinary team review.

An international consensus meeting (Schwarz et al, 2019) suggested that arthroscopic washout can be used to treat acute sepsis of the native knee joint. Potent solutions (eg acetic acid, chlorhexidine, betadine) can be used for arthroscopic washout in prosthetic joint infections, although the exact efficacy of these is not yet known.

Complementary antibiotic therapy is important and helps to stabilise the patient and eradicate infection. However, for antibiotics to be effective, the 6Ds should be followed:

1. Diagnosis: appropriate antibiotics should be given after the identification of organisms with culture and sensitivity
2. Dose: adequate dosage of the antibiotics depending on microbiological advice and the patient's weight
3. Duration: short duration of antibiotics is as effective as longer duration (Li et al, 2019)
4. Duality: ideally combination therapy is given rather than a single antibiotic
5. Delivery: systemic and/or local antibiotics can be used
6. Discuss: it should be mandatory to discuss each case of infection in the multidisciplinary meeting, which should involve orthopaedic surgeons, microbiologists, pharmacists, nurses and orthogeriatricians.

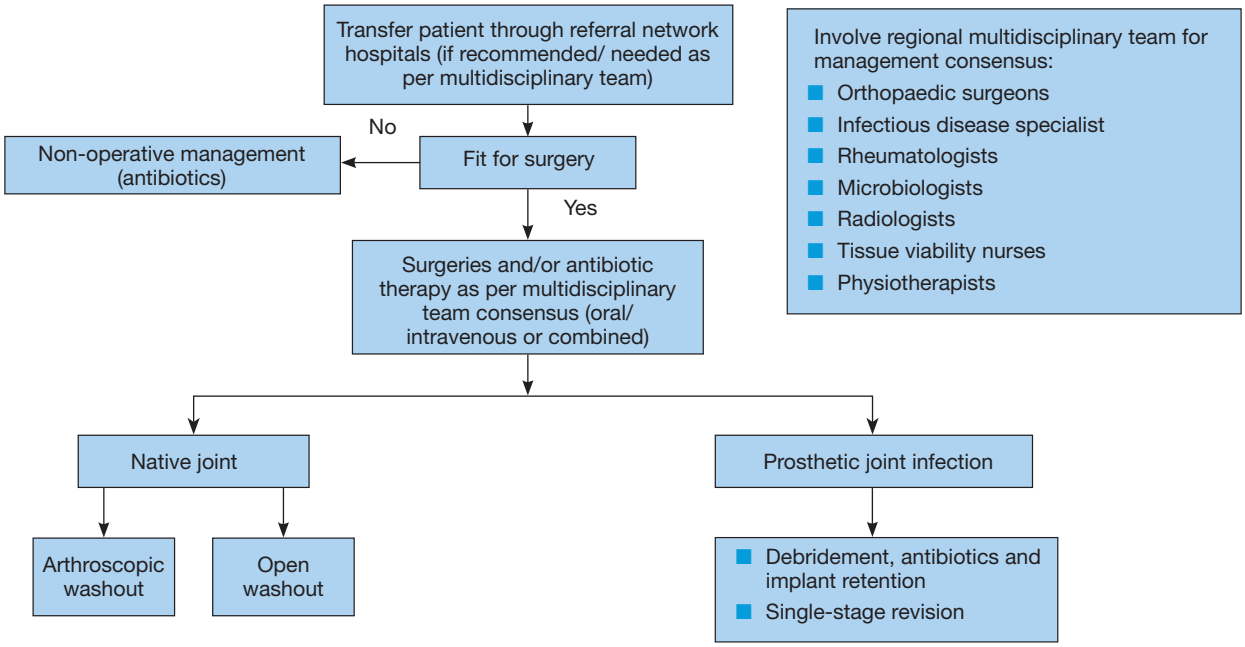

Figure 2. Proposed management of patient with confirmed septic arthritis or prosthetic joint infection.

Surgical treatment

The surgical treatment of septic arthritis is either by arthroscopic or open washout and debridement of the joint. Arthroscopic surgery is preferred for most cases to reduce the bacterial load and relieve the intra-articular pressure, thereby relieving pain. Open surgery is usually performed when there have been multiple failed attempts at arthroscopic surgery, there is severe adhesion in the joint, in small joints where arthroscopic surgery is not possible and in patients with osteomyelitis (Figures 3a–d).

Surgery for prosthetic joint infection varies depending on the extent of infection and the type of prosthesis. Debridement, antibiotics and implant retention is the preferred initial treatment for early prosthetic joint infections, while single-stage or two-stage revision arthroplasty is preferred for late prosthetic joint infections. Amputation is preferred for repeated failed attempts to control infection (Figure 4).

Antibiotic therapy

This should be guided by the causative organism and the antibiotic susceptibility pattern. Some patients may need antibiotic therapy for several weeks or months.

Surgery for septic arthritis or prosthetic joint infection should involve a multidisciplinary team approach. British Orthopaedic Association (2022) guidelines for revision total knee replacement emphasised the need for a multidisciplinary team approach and focus on the volume of revision knee replacements performed by each orthopaedic unit and individual surgeon. The authors suggest that at least 30 revision knee replacements should be performed per unit and 15 per surgeon each year. The aim should be to perform at least 30–100 revision knee replacements per unit per year, to gain expertise in these complex surgeries. The volume of surgery performed for septic arthritis is even smaller than that for prosthetic joint infections.

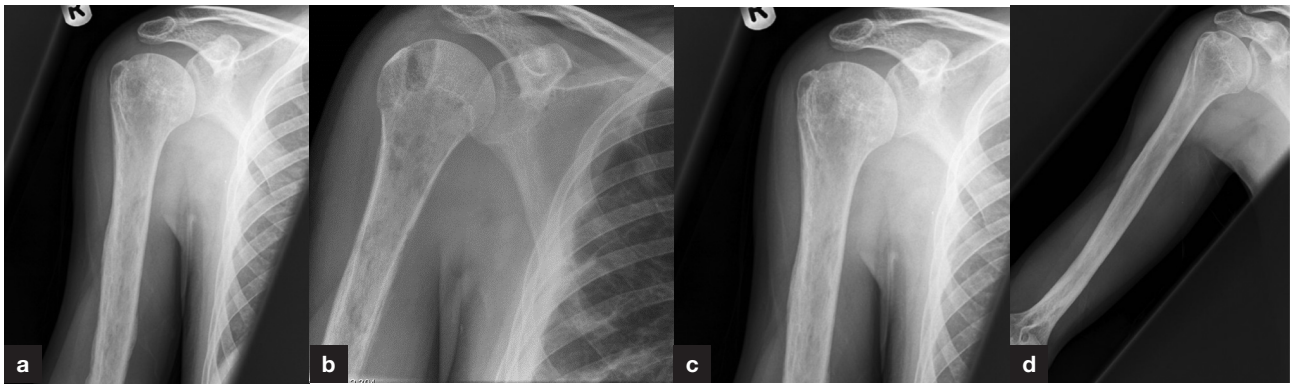

Figure 3. a. Radiograph of an 18-year-old male, with insulin-dependent diabetes mellitus, who was admitted to the intensive therapy unit with sepsis and pan-diaphyseal osteomyelitis. He had life-threatening infection which was treated in intensive therapy unit. Orthopaedic treatment was performed to prevent recurrence and remove the infected material from the humeral shaft by reaming the humeral canal. b. Surgical reaming of the humerus has been performed and infected material removed. c. Radiograph 6 months post-surgery shows improvement with reduced lysis in bone and healing periosteal reaction. d. Radiograph 12 months post-surgery showing near-normal looking humerus.

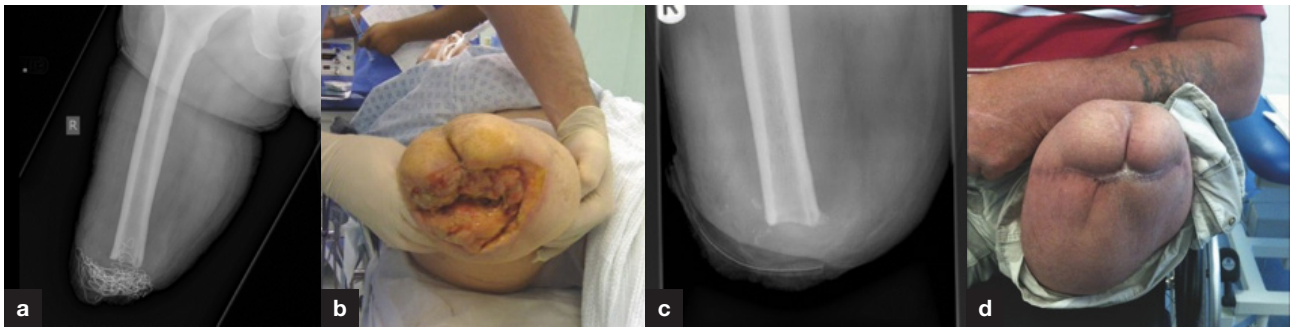

Figure 4. a. Patient with an above-knee amputation for chronic prosthetic joint infection of the knee had recurrence of infection as a result of inadequate initial debridement. This was managed surgically with further debridement and use of negative pressure dressings. b. Infected above-knee amputation stump with a large ulcer. c. Postoperative radiograph of the amputation stump after debridement. d. Healed postoperative amputation stump after debridement and use of negative pressure dressings.

The British Orthopaedic Association (2022) also suggested that the structure of an organisation and coordinated referral pathways between hospitals should be optimised for appropriate care for these patients.

Complications

Alexiou (2022) suggested the following complications of septic arthritis:

1. Antibiotic-associated allergic reaction (medium risk) – the authors believe this is possible but should not be mentioned as the first complication of septic joint treatment
2. Osteomyelitis is another complication which in the authors' experience happens late in septic joints
3. Joint destruction – Alexiou (2022) suggested that if there is irreversible joint damage, then an orthopaedic opinion should be sought regarding surgical solutions for ongoing pain and disability. The authors believe that orthopaedic referral and opinion should be done early in the treatment of septic arthritis and a referral after joint destruction is too late. Getting it Right First Time (https://gettingitrightfirsttime.co.uk/) protocols should be followed to help improve outcomes and save costs.

Conclusions

Surgery is the mainstay of treatment for septic arthritis and prosthetic joint infection. Aspiration should be done for diagnostic purposes only. Complementary antibiotic therapy is important and helps to stabilise the patient and eradicate infection.

Author details

[1]Department of Trauma and Orthopaedics, East Suffolk and North Essex NHS Foundation Trust, UK

[2]Department of Orthopaedics, Schoen Clinic, London, UK

Conflicts of interest

The authors declare that there are no conflicts of interest.

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Key points

- Revision surgery should be delivered by regional networks and cases should be discussed with regional network hospitals and patients transferred if needed.
- Collaborating around a multidisciplinary team meeting should lead to the best decision for the patient.
- Compliance with national standards and guidelines should be mandatory as far as possible.
- Economy of resources and pooling expertise will improve patient management.
- Incentivising best patient care will help improve productivity in hospitals.

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