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Titre : Diagnostic d'infection ostéo-articulaire complexe en réunion de concertation pluridisciplinaire : l'étude PHICTOS

Title: Multidisciplinary team meeting for complex bone and joint infections diagnosis: the PHICTOS study

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Running title: multidisciplinary decision in complex bone and joint infection

Résumé

Objectifs : En France, les infections ostéo-articulaires (IOA) les plus sévères, dites « complexes », doivent être validées en réunion de concertation pluridisciplinaire (RCP) dans un centre de référence. Cependant la définition ministérielle d'IOA complexe a une interprétation clinique potentiellement variable. L'objectif était d'analyser l'accord pour le diagnostic d'IOA complexe, entre experts d'une même RCP et entre RCP de six centres de référence.

Patients et méthodes : Premièrement, cinq experts d'une RCP devaient classer à deux reprises à un mois d'intervalle 24 cas en non-IOA, IOA simple ou IAO complexe, à l'aide du dossier médical. Deuxièmement, six RCP ont validé les 24 mêmes cas, standardisés. Les accords ont été estimés par les coefficients kappa (κ) de Cohen et Fleiss.

Résultats : L'accord inter-expert global était modéré (κ=0,49). Après exclusion des quatre non-IOA, l'accord était médiocre (κ=0,23) ; l'accord intra-expert était modéré (κ=0,50, étendue [0,27-0,90]), non amélioré par l'expérience. L'accord inter-RCP global était modéré (κ=0,58) et semblait plus élevé pour les RCP avec professeur(s) (κ=0,65 vs. κ=0,51), ainsi que celles ayant un temps médian par cas plus long (κ=0,60 vs. κ=0,47). Après exclusion des quatre non-IOA, l'accord global valait κ=0,40.

Conclusions : La première étape a confirmé l'hétérogénéité du classement en IOA complexe selon l'expert. L'accord inter-RCP, qui semblait plus élevé, serait un argument en faveur des RCP, par ailleurs lieu privilégié d'amélioration de l'expertise clinique. Ces résultats, à confirmer, nécessitent d'être complétés par une évaluation de la qualité de la prise en charge et de l'impact medico-économique des RCP.

Abstract:

Background: In France, the most severe bone and joint infections (BJI), called "complex" (CBJI), are assessed in a multidisciplinary team meeting (MTM) in a reference center. However, the definition of CBJI, drawn up by the Health Ministry, is not consensual between physicians. The objective was to estimate the agreement for CBJI classification.

Methods: Initially, five experts from one MTM classified twice, one-month apart, 24 cases as non-BJI, simple BJI or CBJI, using the complete medical record. Secondly, six MTMs classified the same cases using standardized information. Agreements were estimated using Fleiss and Cohen kappa (κ) coefficients.

Results: Inter-expert agreement during one MTM was moderate (κ=0.49), and fair (κ=0.23) when the four non-BJIs were excluded. Intra-expert agreement was moderate (κ=0.50, range 0.27-0.90), not improved with experience. The overall inter-MTM agreement was moderate (κ=0.58), it was better between MTMs with professor (κ=0.65) than without (κ=0.51) and with longer median time per case (κ=0.60) than shorter (κ=0.47). When the four non-BJIs were excluded, the overall agreement decreased (κ=0.40).

Conclusion: The first step confirmed the heterogeneity of CBJI classification between experts. The seemingly better inter-MTM than inter-expert agreement could be an argument in favour of MTMs, which are moreover a privileged place to enhance expertise. Further studies are needed to assess these results as well as the quality of care and medico-economic outcomes after a MTM.

Keywords: bone, complex, infection, joint, multidisciplinary team meeting, agreement

Text:

INTRODUCTION

Bone and joint infections (BJI) have an increasing incidence in Western countries, especially with ageing population and increasing medical conditions [1]. Moreover, the number of arthroplasties, a risk factor of BJI, has been rising over recent decades and is projected to continue to increase, especially in the elderly [1–3].

These device-associated BJIs could potentially lead to complicated management with frequent medical or surgical complications [4–8]. But native BJIs can also require complicated medical care according to the patient's medical conditions [4,6,9–11]. In this context, in 2008 a French health policy designated a number of reference centers for severe cases of BJI, defined as complex BJIs (CBJIs) [12,13]. A national case definition was proposed by the Health Ministry based on clinical (comorbidities), microbiological (antibiotic resistance), and evolution (need for a secondary surgery) criteria [14]. Nine French Reference Centers for CBJIs were implemented nationwide, commissioned to improve medical care, research and organisation in CBJI management, receiving financial and communication support [12]. Each suspected case of CBJI must be checked in a multidisciplinary team meeting (MTM), including a quorum of experts in orthopedics, infectious diseases and microbiology, at a reference center. Indeed, a multidisciplinary approach, involving expertise in orthopedic surgery, infectious diseases, along with plastic and vascular surgery, particularly for complex cases, is now required for success [1] . The multidisciplinary team, which validates the complex nature of the BJI, proposes a medical and/or surgical treatment plan. According to the experts however, the criteria defining CBJI according to the national definition seem to allow a large variability in the diagnosis of CBJIs and thereby in the management, which has never been studied.

The objective of this study was to assess the ratification of the national definition of CBJI, between experts and MTMs of several French reference centers.

PATIENTS AND METHODS

An evaluative study was performed to estimate the agreement between experts and MTMs concerning BJI complexity/severity. First, the agreement between the experts of one MTM was assessed, allowing the selection of the medical records to submit to several MTMs. Second, MTM agreement was tested by conducting a meeting with at least the quorum of experts, where the medical records of the proposed BJI cases were assessed as in a real MTM.

Intra- and inter- expert agreement for CBJI diagnosis in one MTM

Twenty BJI cases were randomly selected in one hospital by running a validated French algorithm of BJI against hospital discharge databases [6]. Four non-BJI cases were randomly added from the orthopedic hospital discharge database.

A double-blind cross-validation was performed by five experts involved in the reference center: two infectious diseases physicians and three orthopedic surgeons, including one fellow, two seniors and two professors. They were first required to individually classify the 24 selected medical records as non-BJI, simple BJI or CBJI by reviewing the medical files, including clinical data, microbiological assays, X-rays and magnetic resonance imaging scans. They then remotely reviewed the same 24 cases individually one month later.

The two-by-two intra- and inter-expert agreements were estimated using the Cohen kappa (κ) coefficient. The overall inter-expert agreement was estimated using the Fleiss κ coefficient for multiple raters.

Inter-MTM agreement for CBJI diagnosis in Six MTMs

The medical records of the 24 cases were standardized by an onsite research assistant from one reference center according to the usual presentation of suspected cases in MTMs. Six multidisciplinary teams reviewed the 24 cases during a MTM. Each MTM had to encompass the quorum of experts (at least one infectious diseases physician, one orthopedic surgeon and one microbiologist) and be conducted as usual, filling a standardized questionnaire leading to the classification of each case into CBJI or not. The item(s) used for CBJI classification, according to the national case definition, were taken from among: surgical issue (complex surgery, amputation, muscle flap, etc.), microbiological issue, specific comorbidities, and prior treatment failure.

The inter-MTM agreement was estimated using Fleiss κ coefficient for multiple raters.

Data collection

A standardized questionnaire was created including the classification of the cases reviewed (non-BJI/ simple BJI / CBJI), BJI patterns of complexity (surgery/microbiology/comorbidity/treatment failure), and time spent by the MTM for each case evaluation.

Information concerning the experts was collected: age, status (fellow, senior, and professor), medical specialty and time since first participation in a MTM.

Statistical analysis

The agreement was estimated for a three-category variable (non-BJI / simple BJI / CBJI) when considering all 24 cases, and for a two-category variable (simple BJI / CBJI) when non-BJI cases were excluded.

Statistical analysis was performed using SAS version 9.3 software for Microsoft Windows (SAS Institute, Cary, NC). The Fleiss κ coefficient was calculated with a specific SAS macro [15]. Cohen κ coefficients were interpreted using Landis and Koch scale: almost perfect $\kappa > 0.80$;

substantial 0.80 - 0.61; moderate 0.60 - 0.41; fair 0.40 - 0.21; slight 0.20 - 0.01; 0.00 no agreement [16].

RESULTS

Intra- and inter- expert agreement for CBJI diagnosis during one MTM

The individual review of the 24 medical records estimated a moderate overall agreement (κ=0.49, corresponding to 10 full agreements). The five experts correctly identified the four non-BJI cases, which were excluded from the inter- and intra-rater agreement estimations.

The overall inter-expert agreement estimated for the 20 BJI cases was fair (κ=0.23, corresponding to six full agreements, one simple BJI and five CBJIs). Two cases were classified identically by four out of five experts. The agreement estimation was improved neither within the same specialty or status, nor between different statuses (Table 1).

When reviewing the 24 cases one month later, the overall intra-rater agreement was moderate (κ-value 0.50, corresponding to between 13 and 19 cases consistently classified). The intra-rater agreement was not dependent upon seniority status (Table 2).

Inter-MTM agreement for CBJI diagnosis in six MTMs

The six participating MTMs fulfilled the legal quorum. The number of participants in one MTM varied from three to five (Table 3), with at least one professor in three MTMs. The participation time in BJI meetings varied from 2 to 26 years, due to the existence of BJI meetings before the implementation of reference centers in several hospitals in France. Each MTM lasted from 87 to 143 minutes (median 106).

The overall agreement in MTM for BJI classification was moderate (κ=0.58, corresponding to 10 full agreements) (Table 4). Three out of four non-BJI cases were correctly identified by all centers'

MTMs, with a substantial agreement for non-BJI/BJI (κ=0.87). When excluding these three cases, the overall agreement was fair (κ=0.40, corresponding to seven full agreements, five simple BJIs and two CBJIs). Seven other cases were classified identically by five out of six centers. Finally, when excluding the same four cases as in the first step, the overall agreement remained fair (κ=0.40).

To assess a potential variability associated with the moment where the decision was made, the agreements of the first 12 cases and the 12 last cases were estimated. These were similar: κ=0.57.

The distribution of criteria leading to CBJI classification according to each MTM and case was varied (Fig.1).

Among the cases classified as CBJI by several MTMs, eight had at least one common criterion of complexity. The main criterion reported was the presence of a comorbidity (15 cases). The main criterion agreement was found for treatment failure, especially its absence, followed by the presence of a surgical complicated situation (Fig.2).

DISCUSSION

This first study assessing the ratification of French CBJI suggests that the MTM agreement in the classification of suspected CBJI was better than individual experts agreement (whatever their status or seniority), although this could not be statistically confirmed. We chose to include a deliberately limited number of cases, to allow the study to be performed by the clinician experts. However, the study suggests that a MTM for CBJI evaluation could limit heterogeneous classification, by gathering experts from different fields, including orthopedists, infectious diseases physicians and microbiologists, as previously shown in literature for other topics [1]. Moreover, the study estimated a fair inter-expert agreement during individual evaluation, which did not increase with experience as expected. One explanation could be that orthopedists and infectious diseases specialists may base their CBJI classification on different criteria, giving a higher disagreement between specialities than seniority. Our study, however, was unable to assess this hypothesis and further qualitative studies should be carried out to evaluate the potential role of MTM composition. Conversely, inter-MTM agreement seemed better than individual agreement and was similar to an evaluative study performed on MTM for parenchymal lung disease [17]. Our study also estimated the median time per case in MTMs, finding a seemingly better agreement when more time was taken for decision-making. Demonstrating the benefit of MTM for the management of CBJI might suggest an improvement in the quality of healthcare in BJI, as previously shown for osteomyelitis management [1]. Indeed, the agreement in case definition by a MTM indirectly involved specific management according to French guidelines for CBJIs.

To our knowledge, the study is the first to assess the agreement for CBJI diagnosis in France according to the definition provided by the French Health Ministry in 2010, though without any gold standard for this diagnosis. To date, no evidence-based study has been performed. As the reference centers have only recently been implemented and exist only in France, CBJIs are a

specifically French topic. The international literature is not currently informative, focusing on prosthetic joint infections reported through national registries, or on healthcare-associated infections which represent only a fraction of CBJIs [18,19]. A French study showed that the management of BJIs was significantly improved after implementing a MTM in an orthopedic surgery unit [20]. Another study showed that MTMs for infection led to improved use of radiological investigation and patient management, cancelling unnecessary investigations, thus saving time and costs [21]. However, CBJI MTMs were not directly targeted. Moreover, due to the heavy workload of physicians who are increasingly called upon to participate in MTMs, to advances in medical technology and national guidelines, and to the time and cost for the hospital, an evaluation of these MTMs is important for future healthcare policy at the local and national level [21–23], to support the reference centers' teams and enhance their position.

This study had some limitations, apart from the limited number of cases as already explained. Non-BJI cases were selected randomly from hospital discharges, which could result in non-discriminating cases. However, one of these non-cases was classified as a CBJI by one MTM, showing the importance of their inclusion. Moreover, an agreement evaluation was performed, excluding these non-BJI cases. Additionally, the individual agreement assessment used non-standardized medical records for expert examination, giving a potential misestimation of the individual and two-by-two expert agreement. Two cases could also have presented an issue: a hand BJI, which could be classified as simple due to the location, and another case where the location targeted by evaluation was unclear. When these two additional cases were excluded, the agreement remained moderate (κ=0.45). However, when the same case was rated twice, intra-expert agreement was only moderate, whereas a high intra-expert agreement was expected, considering the memorisation bias. For reasons of feasibility, each MTM could not remotely review the cases twice. A large-scale review of two cases was, however, performed during the French CBJI congress (79 physicians across France involved in their hospital's CBJI MTM) to individually

classify two BJI cases from our panel as complex or not. The results were similar to the inter-MTM study for both cases. For the case whose complexity gave rise to major debate, the item(s) classifying as CBJI seemed surprisingly more homogeneous than for the case which was classified as complex by a vast majority (supplementary material). However, further studies would be needed to confirm these results.

Performing MTM could help reduce costs due to heterogeneous management, as previously identified for oncology MTMs [24]. Additional analyses must be performed to pursue this interpretation of the impact of MTM on infections, especially BJIs, as insufficient evidence was provided to determine whether MTMs are cost-effective in non-cancer pathologies [25]. For instance, filming during a MTM could allow the decision-making process to be assessed within a qualitative analysis. Moreover, the management of each case checked in MTM could be compared to BJIs managed outside of a MTM to assess the variability of quality of care in order to estimate potential additional costs. Thus, evaluating cost-efficiency could provide major arguments in support of MTMs. Cost-efficiency depends on the strict selection of the cases discussed in MTM to optimise the allocated resources. As every BJI case discussed in a MTM has been registered in a French registry since end of 2012, this study could be carried out, comparing treatments for cases classified as complex versus the non-complex cases reviewed.

Finally, a consensual definition of CBJI currently appears difficult to implement, as very different clinical presentations co-exist, involving the expertise of clinicians from different fields. This confirms the relevance of MTMs for the diagnosis and treatment of these complex cases. Moreover, MTMs are a privileged place to enhance expertise, particularly for the youngest physicians.

This evaluation of MTM in CBJI is the first to date. It supports the current heterogeneity of CBJI classification between clinicians and suggests a better inter-MTM agreement. The reference

centers for CBJI probably improve BJI classification and indirectly management. The quality of healthcare related to MTM conclusions, along with medico-economic outcomes such as cost-efficiency, which were not evaluated in the study, should be assessed by further investigations.

Conflict of interest and funding

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FIGURE LEGENDS:

Figure 1. Patterns of classification in complex bone and joint infection, by multidisciplinary team meeting (MTM).

Figure 2. Number of agreements between multidisciplinary team meetings (MTMs), by classification criterion in complex bone and joint infection.

TABLE LEGENDS:

Table I. Two-by-two expert agreement in classification of bone and joint infections (5 experts)
Table II. Intra-rater agreement after a one-month interval - kappa (κ) coefficient
Table III. Characteristics of reference center members
Table IV. Agreement between reference centers – kappa (κ) coefficients

FIGURES

FIGURE 1

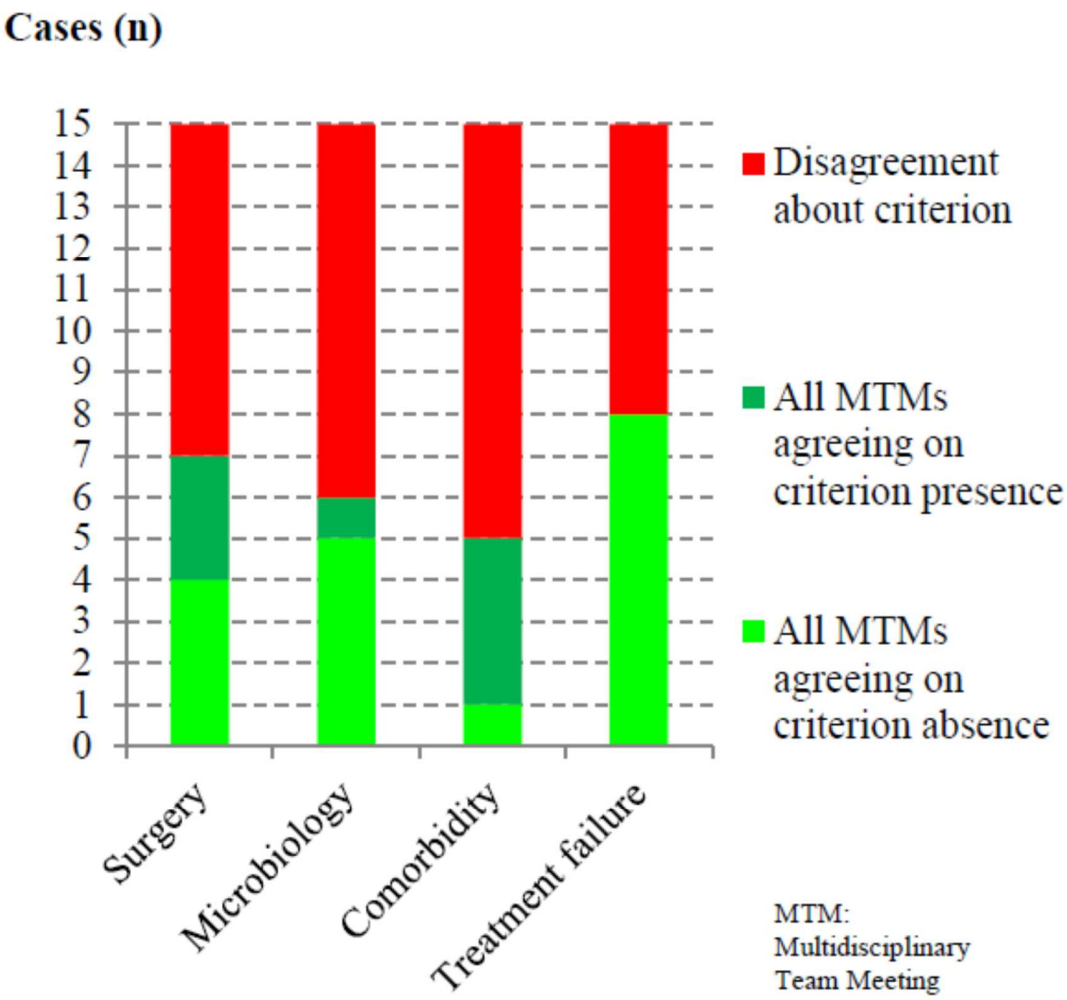
Cases (n)
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
Disagreement about criterion
All MTMs agreeing on criterion presence
All MTMs agreeing on criterion absence
Surgery
Microbiology
Comorbidity
Treatment failure
MTM: Multidisciplinary Team Meeting

Figure 2

TABLES

Table 1. Two-by-two expert agreement in classification of bone and joint infections (5 experts)

	Specialty agreement			Status agreement				
Number of pairs (p)	3p	1p	6p	1p	1p	4p	2p	2p
Experts	Orthop.	Infect.	Orthop. Vs Infect.	Professors	Seniors	Professor vs Senior	Professor vs Fellow	Senior vs Fellow
Kappa min.	0.00	0.06	0.13	0.21	0.21	0.06	0.00	0.50
Kappa max.	0.50		0.50			0.26	0.40	0.50

Kappa agreement evaluation: 0.00: no agreement – 0.01-0.20 ! slight – 0.21-0.40 : fair – 0.41-0.60 : moderate – 0.61-0.80 : substantial - >0.80 : almost perfect

Table 2. Intra-rater agreement after a one-month interval – kappa (K) coefficients

Expert	**Estimation (K)**
Professor 1	Moderate (0.47)
Professor 2	Fair (0.27)
Senior 1	Almost perfect (0.90)
Senior 2	Fair (0.31)
Fellow	Moderate (0.50)

Table 3. Characteristics of reference centre members

MTM members	Reference centre					
	A	B	C	D	E	F
Members (n)	5	4	5	4	3	3
Status						
• Professor	2				2	2
• Senior	3	2	4	4	1	1
• Fellow		2	1			
Medical specialty						
• Infectiology	2	2	1	1	1	1
• Orthopaedy	2	1	2	1	1	1
• Microbiology	1	1	1	1	1	1
• Rheumatology			1	1		
Age*	40 (39-63)	44.5 (31-60)	46 (33-51)	-	57 (53-67)	44 (51-60)
MD exercise*	12 (10-30)	14 (2-31)	16 (3-22)	17.5 (5-20)	38 (25-40)	>20 (14->20)
Participation in MTM*	8 (8-8)	5.5 (2-8)	8 (3-8)	8 (5-8)	20 (7-26)	6 (6-6)
Mean time per case (minutes)	2.5	3.5	3.5	5	4	5

*Years, median (min-max)

MD : Medical doctor

MTM : Multidisciplinary Team Meeting

Table IV. Agreement between reference centres – kappa (κ) coefficients

Reviewed charts in the multidisciplinary team meetings	MTM (n)	Agreement estimation (kappa κ)	
		All (n=24)	BJI* (n=21)
All MTMs	6	Moderate (0.58)	Fair (0.40)
3 members	2	Moderate (0.47)	Fair (0.24)
4 members	2	Moderate (0.41)	Slight (0.14)
5 members	2	Moderate (0.45)	Fair (0.22)
Professor	3	Substantial (0.65)	Moderate (0.49)
No professor	3	Moderate (0.51)	Fair (0.30)
Median time/case ≥ 4mn	3	Moderate (0.60)	Moderate (0.42)
Median time/case < 4mn	3	Moderate (0.47)	Fair (0.24)

** excluding 3 non-BJIs recognized by all reference centres*

BJI: Bone and Joint Infection; MTM: Multidisciplinary Team Meeting