Does the alpha-defensin lateral flow test conserve its diagnostic properties in a larger population of chronic complex periprosthetic infections? Enlargement to 112 tests, from 42 tests in a preliminary study, in a reference center.

Benoît de Saint Vincent, Pierre Martinot, Adrien Pascal, Eric Senneville, Caroline Loiez, Gilles Pasquier, Julien Girard, Sophie Putman, Henri Migaud

Version of Record: https://www.sciencedirect.com/science/article/pii/S1877056821001316
Manuscript_ffdcf0d7ffcf157184a5d60888044e98

Follow-up / Review article

Does the alpha-defensin lateral flow test conserve its diagnostic properties in a larger population of chronic complex periprosthetic infections? Enlargement to 112 tests, from 42 tests in a preliminary study, in a reference center

Benoît **de Saint Vincent** [a,b,c,*], Pierre **Martinot** [a,b,c], Adrien **Pascal** [a,b,c], Eric **Senneville** [a,b,d], Caroline **Loiez** [a,b,e], Gilles **Pasquier** [a,b,c], Julien **Girard** [a,b,c,f], Sophie **Putman** [a,b,c], Henri **Migaud** [a,b,c]

a Centre de Référence pour le Traitement des Infections Ostéo-Articulaires Complexes (CRIOAC), Avenue du Professeur-Émile-Laine, 59037 Lille, France
b Univ. Lille, CHU Lille, ULR 4490, Département Universitaire de Chirurgie Orthopédique et Traumatologique, F-59000 Lille, France
c Service d'Orthopédie, Hôpital Salengro, Place de Verdun, CHU Lille, F-59000 Lille, France
d Service de Maladie Infectieuses et du Voyageur, CH Dron, Rue du Président-Coty, 59208 Tourcoing, France
e Service de Bactériologie–Hygiène, Centre de Biologie-Pathologie, CHU de Lille, 59000 Lille, France
f Département de Médecine du Sport, Faculté de Médecine de Lille, Université de Lille 2, 59045 Lille, France
* **Corresponding author**: Benoît de Saint Vincent,
Centre de Référence pour le Traitement des Infections Ostéo-Articulaires Complexes (CRIOAC), Avenue du Professeur-Émile-Laine, 59037 Lille-Tourcoing, France
E-mail: benoitdesaintvincent@gmail.com

Abstract

Background

Diagnosis of periprosthetic infection (PPI) is crucial for management of bone and joint infection. The preoperative gold-standard is joint aspiration, providing results after 2-14 days' culture, with non-negligible false negative rates due to the fragility of certain micro-organisms and/or prior antibiotic treatment. The Synovasure™ alpha-defensin lateral flow test (Zimmer, Warsaw, IN, USA) contributes within minutes to

joint fluid diagnosis of almost all infectious agents, including in case of concomitant antibiotic therapy. Validity remains controversial, notably in complex microbiological situations: multi-operated patients, diagnostic doubt despite iterative sterile culture, long-course antibiotic therapy. We extended a prospective study reported in 2018, to determine whether the test maintained diagnostic value in a larger population, assessing 1) negative (NPV) and positive (PPV) predictive value, and 2) sensitivity and specificity.

Hypothesis

Synovasure™ maintains NPV above 95% in a broader population of microbiologically complex suspected PPI.

Material and methods

Synovasure™'s performance was assessed between October 2015 and October 2019 in 106 patients (112 tests) in complex diagnostic situations: 37 discordant cultures (discordant findings between 2 samples), 65 cases with clinically or biologically suspected infection but iterative sterile culture, 10 emergencies (requiring surgery, precluding antibiotic window, or mechanical failure in suspected infection), including 5 with ongoing antibiotic therapy for infection in another organ. Six tests were repeated in the same patient and same joint at >6 months' interval for strong clinical suspicion of infection. The main endpoint was the MSIS score (MusculoSkeletal Infection Society, 2018).

Results

NPV was 98.8%, PPV 72.4%, sensitivity 95.5% and specificity 91%. Prevalence of infection was 19.6%. Only 1 of the 22 infected patients had negative Synovasure™ tests, compared to 81 of the 84 non-infected patients.

Conclusion

Synovasure™ is a reliable novel diagnostic test, contributing mainly to ruling out infection thanks to its strong NPV. The cost imposes sparing use, but medico-economic assessment would be worthwhile.

Level of evidence: III; prospective of diagnostic performance.

Key-words: Periprosthetic infection, Synovasure, alpha defensin, MSIS, infection diagnosis, bone and joint infection

1. Introduction

Periprosthetic infection (PPI) requires fast and reliable diagnosis [1,2] to enable adapted treatment with favorable functional and economic outcome [3,4]. The preoperative gold-standard examination is joint aspiration [5–8], but sometimes requires 14 days' culture to provide results and shows a non-negligible rate of false negatives [6,9,10], notably due to infectious agents that are difficult to reveal or to concomitant antibiotic therapy.

The 2018 update of the Musculoskeletal Infection Society (MSIS) bone and joint infection diagnostic criteria provided clarification [9,11] (Table 1), with some minor new criteria. Joint alpha-defensin assay, in the laboratory or by rapid detection test (RDT), is one of the new criteria for positive diagnosis [9-11]. Following our previous study including 42 tests, RDT has shown good reliability in difficult diagnoses in our reference center.

Many studies assessed performance, but few with more than 100 cases, and most were designer studies or meta-analyses [8,12-17], sometimes including non-complex microbiological situations. We therefore sought to confirm our initial findings on 42 tests in a wider population of >100 patients with suspected complex PPI, and updated our series to 112 tests. The aim was to assess, in this larger sample: 1) negative (NPV) and positive (PPV predictive value, and 2) sensitivity and specificity. The study hypothesis was that the Synovasure™ RDT would maintain above 95% NPV in the larger population of suspected microbiologically complex PPI.

2. Material and methods

2.1 Patients

Samples were taken between October 2015 and October 2019 in the Complex Bone and Joint Infection Reference Center (CRIOAC) of Lille-Tourcoing, France, using Synovasure™ (Zimmer, Warsaw, IN) at assessment ahead of surgery in theater. The

main endpoint was infection on the 2011 MSIS criteria as updated in 2018 [9] (Table 1).

112 Synovasure™ tests were made in 106 patients (58 men, 48 women; age, 24-92 years), for the following: 37 discordant cultures, 65 cases with clinically or biologically suspected infection but repeated sterile culture, and 10 emergencies, including 5 with ongoing antibiotic therapy without possibility of antibiotic window (infection in another organ) (Table 2). Emergencies were defined as need for surgery without antibiotic window or for mechanical failure in suspected infection. Forty-eight patients (42.9%) had history of infection in the same joint, and 35 (31.6%) had history of wound problems following index arthroplasty. Thirty-two patients (28.5%) had been referred for a second opinion following diagnostic failure in the referring institution. Most cases concerned multi-operated joints, 88 (78.6%) with history of at least 2 arthrotomies (mean, 3.3 ± 2; range, 1-14). There were 59 knee and 39 hip replacements, 4 total femur replacements, 3 hip resurfacings, and 1 patellofemoral implant. RDT was performed at a mean 24.7 ± 28.5 months (range, 3-168 months) post-arthroplasty. No RDTs were repeated in the previous study.

2.2 Method

The methodology of the previous study [12] was continued. The test was performed in included patients at the time of preoperative joint aspiration in the operating room. The kit used a small amount of joint fluid to give a result in 10 minutes. Joint fluid was also sent for bacteriological analysis.

2.3 Assessment

The 112 test results were compared against MSIS PPI diagnostic criteria after validation in a multidisciplinary team meeting. The 2018 criteria include alpha defensin test as a minor criterion, unlike in the 2013 version, without change in the other diagnostic criteria.

2.4 Statistics

Negative (NPV) and positive (PPV) predictive value, sensitivity and specificity were calculated. The main endpoint (infection: yes/no) was based on MSIS criteria. One

positive Synovasure™ result associated with metallosis identified macroscopically was discarded.

3. Results

NPV was 98.8%, PPV 72.4%, sensitivity 95.5% and specificity 91% (Table 3).

Prevalence of infection was 19.6% (22/112). Twenty-one of the 22 infected patients had positive Synovasure™, while 81 of the 84 non-infected patients had negative Synovasure™ (Table 3). Six patients had a second test following a negative result with more than 6 months' poor progression. Figure 1 shows the study flowchart.

Forty-eight patients had multiple operative samples taken, 29 of which were sterile and 19 showed 1 or several microorganisms (Table 4).

Comparing the RDT with aspiration culture, 98 Synovasure™ results (87.5%: 98/112) were concordant with aspiration culture; all 82 negative results were associated with sterile culture (100%), and 16 of the 29 positive tests, excluding the case of metallosis (55.2%) were associated with positive culture (Table 5).

4. Discussion

The present study confirmed the findings of our previous study, with high negative and positive predictive values: 96.7% and 72.7% respectively in the first report, and 98.8% and 72.4% in the present larger population. Sensitivity and specificity were also high: 88.9% and 90.6% respectively in the first report, and 95.5% and 91% in this series at last follow-up, in line with the literature [13–18]. None of the patients in the former series were re-tested. The former results doubtless contributed to the alpha-defensin test being included in the 2018 MSIS diagnostic criteria [9]. Amanatullah et al. [19] warned against using alpha-defensin routinely and in simple cases. However, the high NPV of Synovasure™ greatly enhanced the diagnostic armamentarium for PPI. It is less effective than laboratory assay of alpha-defensin, but adds the rapidity of RDT to the reliability of assay [14,16]. Even in the most complex cases, it can rule out infection, and thus provides a criterion of diagnostic elimination. This is why it was more often implemented in emergency (8.9%) in the present more recent study. Testing must, however, strictly adhere to the correct

procedure, to avoid error due to misuse: e.g., macroscopic metallosis in the joint fluid, a ≤2 month interval since index surgery, or sample dilution [20–23].

In PPI in the most microbiologically complex situations, diagnosis requires multiple evidence. Samples and cultures are the most important, and are major criteria for MSIS 2018 [9], but are not always available, notably in case of concomitant antibiotic therapy. Here, multiple minor criteria are needed for diagnosis. Including Synovasure™ and exploring new diagnostic combinations go towards meeting this need [8,24–27]. As well as being a major criterion, culture is indispensable to identify culprit microorganisms and draw up an adapted antibiogram. Detecting alpha-defensin on Synovasure™ is a minor MSIS criterion, but is highly advantageous in case of prior or ongoing antibiotic therapy.

For reasons of cost, we reserved the test for microbiologically complex situations: multi-operated patients (mean 3.3 ± 2.4 arthrotomies), all with uncertain microbiological diagnosis, including 5 (out of 112) with ongoing antibiotic therapy. Thirty-two cases were referrals after failure of treatment in the referring centers; 48 had history of infection. Causes of false positives (metallosis, or interval since index surgery ≤2 months) [22,23] or false negatives (sample dilution) [21] need to be known, to avoid faulty use of the test and diagnostic error. There is also a medico-economic issue [3,28], as Synovasure™ should doubtless be reserved to complex cases in view of its cost; however, when it is able to rule out infection, this is to be weighed against the costs of hospital stay and antibiotics. The leukocyte esterase test is cheaper but is unsuited in case of hemarthrosis, which is not in practice uncommon [7,8]. In case of hemarthrosis, centrifugation of synovial fluid can make the leukocyte esterase test feasible, but is difficult, especially in cases of hip prosthesis, where the amount of fluid is often small.

The present study shared certain limitations with the previous one, the protocol being the same. 1) It was a prospective cohort follow-up study. The complexity of the target population ruled out constituting a control group, which in any case would not help test performance assessment. 2) Diagnostic classification on MSIS score may induce bias inherent to the method in case of negative preoperative culture. Test detection parameters are known to vary according to the classification used [29]. On the other hand, all cases were validated in the multidisciplinary team meeting, which

should limit classification bias. 3) The population was rather heterogeneous, but this matches the intake in reference centers, which includes the most microbiologically complex cases, which are the most difficult for testing to decipher; this in fact reinforces the study's external validity. Likewise, enlarging the study population enhanced the robustness of the results, strengthening external validity, especially regarding test performance in case of ongoing antibiotic therapy, where the sample increased from just 1 to 5 cases.

5. Conclusion

The Synovasure™ RDT is a reliable new diagnostic instrument in PPI, even in microbiologically complex situations. Its high cost imposes selective use. It cannot replace culture, which identifies microorganisms and their resistance profiles. The high NPV of the test enables it to rule out infection, thereby reducing hospital stay and use of antibiotics.

Disclosure of interest: Henri Migaud is Editor in Chief of Orthopaedics & Traumatology: Surgery & Research, and, elsewhere, is an educational and research consultant for Zimmer, Tornier-Corin, SERF and MSD. Gilles Pasquier is, elsewhere, an educational and research consultant for Zimmer-Biomet. Julien Girard elsewhere, is an educational and research consultant for Microport, Smith & Nephew and Corin. Eric Senneville is, in speaker for Zimmer and, elsewhere, a speaker for Sanofi-Aventis, Astra-Zeneca and Gilead and consultant for Novartis, Pfizer and MSD. Sophie Putman is, elsewhere, a consultant for Tornier-Corin. The other authors have no conflicts of interest to disclose.

Funding: In-house funding from the Lille-Tourcoing complex bone and joint infection reference center (CRIOAC); no other funding.

Author contributions: Benoît de Saint Vincent**:** data acquisition, analysis and

interpretation; article writing. Pierre Martinot: article writing, and critical revision for intellectual content. A. Pascal: data acquisition. E. Senneville: data analysis and coordination of decisions as coordinator of the Lille-Tourcoing CRIOAC. C. Loiez: microbiological analyses. G. Pasquier and J. Girard: sampling and surgery. S. Putman: coordination of article writing, analysis and statistics.

References

[1] Li C, Renz N, Trampuz A, Ojeda-Thies C. Twenty common errors in the diagnosis and treatment of periprosthetic joint infection. Int Orthop 2020;44:3–14.

[2] Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2013;56e1-e25.

[3] Romanò CL, Trentinaglia MT, De Vecchi E, Logoluso N, George DA, Morelli I, et al. Cost-benefit analysis of antibiofilm microbiological techniques for peri-prosthetic joint infection diagnosis. BMC Infect Dis 2018;18:154. https://doi.org/doi: 10.1186/s12879-018-3050-8.

[4] Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic Burden of Periprosthetic Joint Infection in the United States. J Arthroplasty 2012;27:61–5.

[5] Hassebrock JD, Fox MG, Spangehl MJ, Neville MR, Schwartz AJ. What is the role of repeat aspiration in the diagnosis of periprosthetic hip infection? J Arthroplasty 2019;34:126–31.

[6] Newman JM, George J, Klika AK, Hatem SF, Barsoum WK, Trevor North W, et al. What is the diagnostic accuracy of aspirations performed on hips with antibiotic cement spacers? Clin Orthop Relat Res 2017;475:204–11.

[7] Fernández-Sampedro M, Fariñas-Alvarez C, Garces-Zarzalejo C, Alonso-Aguirre MA, Salas-Venero C, Martínez-Martínez L, et al. Accuracy of different diagnostic tests for early, delayed and late prosthetic joint infection. BMC Infect Dis 2017;17:592. https://doi.org/doi: 10.1186/s12879-017-2693-1.

[8] Arvieux C, Common H. New diagnostic tools for prosthetic joint infection. Orthop Traumatol Surg Res 2019;105 Suppl 1:S23–30.

[9] Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, et al. The 2018 Definition of periprosthetic hip and knee infection: An evidence-based and validated

criteria. J Arthroplasty 2018;33:1309-1314.e2.

[10] Bauer T, Roux A-L, Dinh A. What's new in periprosthetic joint infection: Diagnosis and bacteria. Orthop Traumatol Surg Res 2018;104:425–6.

[11] Abdelaziz H, Rademacher K, Suero EM, Gehrke T, Lausmann C, et al. The 2018 International Consensus Meeting Minor Criteria for Chronic Hip and Knee Periprosthetic Joint Infection: Validation From a Single Center. J Arthroplasty 2020;35:2200-2203.

[12] de Saint Vincent B, Migaud H, Senneville E, Loiez C, Pasquier G, Girard J, et al. Diagnostic accuracy of the alpha defensin lateral flow device (Synovasure) for periprosthetic infections in microbiologically complex situations: A study of 42 cases in a French referral centre. Orthop Traumatol Surg Res 2018;104:427–31.

[13] Gehrke T, Lausmann C, Citak M, Bonanzinga T, Frommelt L, Zahar A. the accuracy of the alpha defensin lateral flow device for diagnosis of periprosthetic joint infection: Comparison with a gold standard. J Bone Joint Surg Am 2018;100:42–8.

[14] Eriksson HK, Nordström J, Gabrysch K, Hailer NP, Lazarinis S. Does the alpha-defensin immunoassay or the lateral flow test have better diagnostic value for periprosthetic joint infection? A meta-analysis. Clin Orthop Relat Res 2018;476:1065–72.

[15] Kleiss S, Jandl NM, Novo de Oliveira A, Rüther W, Niemeier A. Diagnostic accuracy of alpha-defensin enzyme-linked immunosorbent assay in the clinical evaluation of painful hip and knee arthroplasty with possible prosthetic joint infection. Bone Joint J 2019;101:970–7.

[16] Marson BA, Deshmukh SR, Grindlay DJC, Scammell BE. Alpha-defensin and the Synovasure lateral flow device for the diagnosis of prosthetic joint infection: a systematic review and meta-analysis. Bone Joint J 2018;100:703–11.

[17] Bonanzinga T, Zahar A, Dütsch M, Lausmann C, Kendoff D, Gehrke T. How Reliable Is the Alpha-defensin Immunoassay Test for Diagnosing Periprosthetic Joint Infection? A Prospective Study. Clin Orthop Relat Res 2017;475:408-415.

[18] Kuiper JWP, Verberne SJ, Vos SJ, van Egmond PW. Does the Alpha Defensin ELISA Test Perform Better Than the Alpha Defensin Lateral Flow Test for PJI Diagnosis? A Systematic Review and Meta-analysis of Prospective Studies. Clin Orthop Relat Res 2020;478:1333-1344.

[19] Amanatullah DF, Cheng RZ, Huddleston Iii JI, Maloney WJ, Finlay AK, et al. The routine use of synovial alpha-defensin is not necessary. Bone Joint J 2020;102:593-599.

[20] Deirmengian C, Kardos K, Kilmartin P, Gulati S, Citrano P, Booth RE. The Alpha-defensin test for periprosthetic joint infection responds to a wide spectrum of organisms. Clin Orthop Relat Res 2015;473:2229–35.

[21] Deirmengian C, Feeley S, Kazarian GS, Kardos K. Synovial fluid aspirates diluted with saline or blood reduce the sensitivity of traditional and contemporary synovial fluid biomarkers. Clin Orthop Relat Res 2020;In press. doi: 10.1097/CORR.0000000000001188.

[22] Plate A, Stadler L, Sutter R, Anagnostopoulos A, Frustaci D, Zbinden R, et al. Inflammatory disorders mimicking periprosthetic joint infections may result in false-positive α-defensin. Clin Microbiol Infect 2018;24:1212.e1-1212.e6.

[23] Partridge DG, Gordon A, Townsend R. False-positive synovial fluid alpha-defensin test in a patient with acute gout affecting a prosthetic knee. Eur J Orthop Surg Traumatol 2017;27:549–51.

[24] Deirmengian C, Kardos K, Kilmartin P, Cameron A, Schiller K, Parvizi J. Combined measurement of synovial fluid α-Defensin and C-reactive protein levels: highly accurate for diagnosing periprosthetic joint infection. J Bone Joint Surg Am 2014;96:1439–45.

[25] Achermann Y, Vogt M, Leunig M, Wüst J, Trampuz A. Improved diagnosis of periprosthetic joint infection by multiplex PCR of sonication fluid from removed implants. J Clin Microbiol 2010;48:1208–14.

[26] Ettinger M, Savov P, Calliess T, Windhagen H, Lichtinghagen R, Lukasz A, et al. Improved diagnostic accuracy with the classification tree method for diagnosing low-

grade periprosthetic joint infections by quantitative measurement of synovial fluid alpha-defensin and C-reactive protein. Int Orthop 2020;44:31–8.

[27] Ronde-Oustau C, Diesinger Y, Jenny JY, Antoni M, Gaudias J, Boeri C, et al. Diagnostic accuracy of intra-articular C-reactive protein assay in periprosthetic knee joint infection--a preliminary study. Orthop Traumatol Surg Res 2014;100:217–20.

[28] Graves N, Wloch C, Wilson J, Barnett A, Sutton A, Cooper N, et al. A cost-effectiveness modelling study of strategies to reduce risk of infection following primary hip replacement based on a systematic review. Health Technol Assess 2016;20:1-144; 2016.

[29] Huard M, Detrembleur C, Poilvache H, et al. Alpha Defensin: A Diagnostic Accuracy Depending on the Infection Definition Used. J Arthroplasty 2020;35:1355-1360.

Table 1 - MusculoSkeletal Infection Society (MSIS) 2018 criteria (see Excel file)

Table 2 - Causes underlying emergency Synovasure test

Causes	Number of cases
Spontaneous hematoma with sudden pain with no context of trauma	2
Painful mechanical valve and joint and history of sepsis; absence of recurrence checked before emergency heart surgery	2
Immunodepression with inflammatory syndrome; history of sepsis, controlled before continuation of immunodepression	1
Spontaneous hematoma needing evacuation; antibiotics for general cause	1
Ongoing antibiotic therapy for endocarditis on cardiac valve, interruption not feasible; screening for joint entry point before attempting valve surgery	2
Bacteremia at digestive entry point, treated but with residual joint pain	1
Treated erysipelas; screening for underlying joint infection	1

Table 3 - Synovasure performance

Performance of Synovasure™ test	MSIS indicating infection	MSIS ruling out infection
Synovasure Positive	21 Sensitivity: 95.5%	8* PPV: 72.4%
Synovasure Negative	1 NPV: 98.8%	81 Specificity: 91%

* One case of positive Synovasure™ test with metallosis identified on macroscopic joint fluid aspect, excluded from analysis

PPV: positive predictive value; NPV: negative predictive value

Table 4 - Isolates.

Microorganisms identified intraoperatively*	
S. epidermidis	9
S. aureus	2
S. capitis	2
S. caprae	1
S. lugudunensis	1
S. haemolyticus	1
S. piscifermetans	1
Granulicatella adiacens	1
E.coli	1
P. aeruginosa	2
Acidovorax temperans	1
Candida parapsilosis	1
Polymicrobial	3

Microorganisms identified preoperatively (n =3 patients)	
S. epidermidis	1
E.coli	1
C. acnes	1

* 48 operative samples: 29 sterile, 19 non-sterile

Table 5 - Concordance between Synovasure™ and culture of preoperative samples

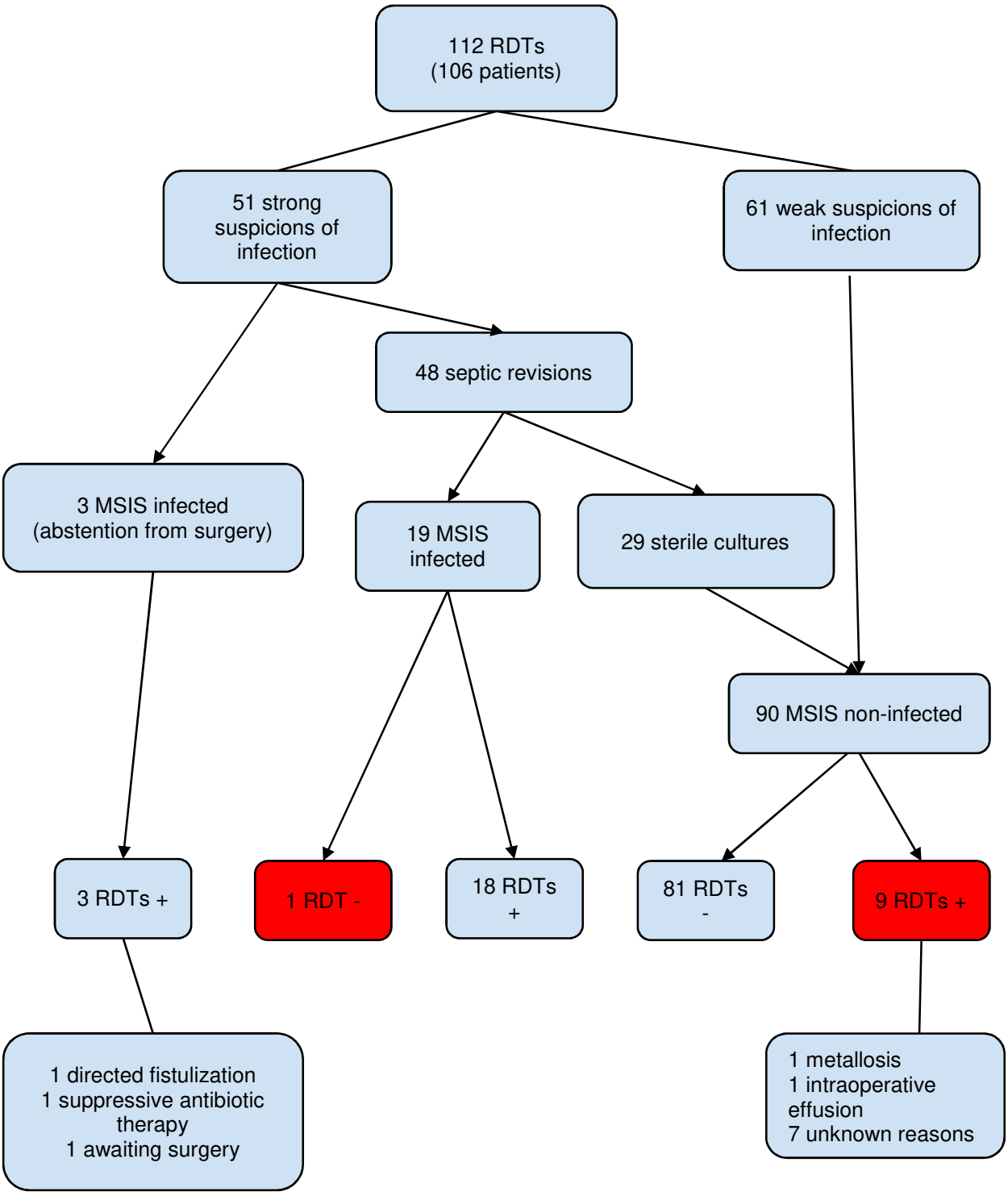
Identical	98 (87.5%)
Negative test with sterile culture	82 (100%)
Positive test with non-sterile culture	16 (55.2%)

* One case of positive Synovasure™ test with metallosis identified on macroscopic joint fluid aspect, excluded from analysis

Figure legend

Figure 1: Study flowchart.

Figure 1.


112 RDTs
(106 patients)
51 strong suspicions of infection
61 weak suspicions of infection
48 septic revisions
3 MSIS infected
(abstention from surgery)
19 MSIS infected
29 sterile cultures
90 MSIS non-infected
3 RDTs +
1 RDT -
18 RDTs +
81 RDTs -
9 RDTs +
1 directed fistulization
1 suppressive antibiotic therapy
1 awaiting surgery
1 metallosis
1 intraoperative effusion
7 unknown reasons

Major criteria (at least one of the following)	Decision
Two postive cultures of the same organism	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

			Threshold		Score	Decision
	Minor Criteria		Acute infection	Chronic infection		
Preoperative Diagnosis	Serum	Elevated CRP (mg/L) or Elevated D-Dimer (µg/L)	>100 NA	>10 >860	2	≥6 Infected
		Elevated ESR (mm/h)	NA	>30	1	
	Synovial	Elevated synovial WBC count (cell/µL) or Leukocyte esterase test (from urine test strip)	>10000 ++ (or more)	>3000 ++ (or more)	3	**2-5 Possibly Infected** (require the inclusion of intraoperative findings for confirming the diagnosis)
		Alpha-Defensin (signal-to-cutoff ratio)	>1	>1	3	
		Elevated synovial PMN (%)	>90	>70	2	
		Elevated synovial CRP (mg/L)	NA	>6.9	1	0-1 Not Infected

			Score	Decision (pre-op score + intraoperative findings)
Intraoperative diagnosis	Possibly Infected (according to pre-op score) OR Dry tap		Score	Decision (pre-op score + intraoperative findings)
	Preoperative score		-	≥6 Infected
	Intraoperative Findings	Positive histology	3	**4-5 Inconclusive** (consider further molecular diagnostic)
		Positive purulence (without metallosis)	3	
		Single positive culture	2	≤3 Not Infected