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Percutaneous Image-guided Biopsy of the Spleen: Systematic Review and Meta-Analysis of the Complication Rate and Diagnostic Accuracy[1]

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Purpose: To use meta-analysis to determine the complication rate and diagnostic accuracy of image-guided percutaneous needle biopsy of the spleen.

Materials and Methods: Several electronic databases were searched through July 2010 without language restrictions. Two reviewers independently selected studies that met the inclusion criteria for the diagnostic accuracy and complication rate arms of the study. Study data were independently extracted by the two reviewers. The primary 2 × 2 data were investigated with a random-effects meta-analysis of sensitivity and specificity. The complication rate data were investigated with a random-effects meta-analysis; sensitivity analysis of complication rate, excluding needles larger than 18 gauge, was performed.

Results: Four studies met the inclusion criteria for the diagnostic accuracy arm (639 patients), and nine met the inclusion criteria for the complication rate arm (741 patients). The meta-analysis showed a pooled sensitivity of 87.0% (95% confidence interval [CI]: 80.7%, 91.4%) and specificity of 96.4% (95% CI: 81.4%, 99.4%). The pooled major complication rate was 2.2% (95% CI: 0.8%, 5.6%). Sensitivity analysis with the removal of biopsies performed with needles larger than 18 gauge showed a major complication rate of 1.3% (95% CI: 0.6%, 2.5%). The most commonly encountered complications were hemorrhage followed by pain.

Conclusion: Image-guided percutaneous biopsy of the spleen demonstrates high diagnostic accuracy and a major complication rate, for needles 18 gauge or smaller, that is similar to that reported for the liver and kidney. This technique should be considered a favorable alternative to splenectomy.

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The spleen is an organ that is not commonly affected by disease; however, those that do affect the spleen are myriad, including malignancy (lymphoma, metastatic disease), infection (tuberculosis, fungal), and infiltrative processes such as sarcoidosis (1–4). Because imaging has not been demonstrated to be accurate for diagnosis, tissue samples from the spleen may be required to stage or diagnose malignancy or to assess for possible infection (1,2). Tissue samples can be obtained either by using splenectomy or percutaneous biopsy (2,5–7). Splenectomy carries a relatively high reported morbidity (8.6%–37%) and mortality (0%–2.9%) rate, primarily because of infection (7–9). Percutaneous biopsy, which has reported complication rates as low as 0.5% for organs such as the liver and kidney, is a potentially safer alternative (10–13).

Historically, image-guided percutaneous biopsy of the spleen has been approached with trepidation by radiologists because of concerns regarding accessibility and risk of hemorrhage (14). This reluctance may be related to an early report of a high major complication rate (13%) for percutaneous biopsy of the spleen performed with a 14-gauge needle (15). Several more recent publications have reported much lower complication rates with smaller needle diameters (18 gauge or smaller) (5,6,16). Diseases that commonly affect the spleen can pose a diagnostic challenge to the clinician, radiologist, and pathologist, and the reported diagnostic accuracy of splenic biopsy varies, ranging between 84% and 90% (5,14,16–21).

Advances in Knowledge

- Splenic biopsy performed with needles 18 gauge or smaller has a major complication rate comparable with that for other abdominal organs such as the liver and kidney.
- Splenic biopsy has a favorable complication rate compared with splenectomy.
- Splenic biopsy has a high overall diagnostic accuracy.

The purpose of this systematic review and meta-analysis was to determine the complication rate and diagnostic accuracy of image-guided percutaneous needle biopsy of the spleen in adult patients suspected of having disease of the spleen.

Materials and Methods

This meta-analysis and systematic review was written by using the guidelines outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (22,23). The protocol of this study was not published elsewhere. Because the diagnostic accuracy and complication rate of image-guided percutaneous biopsy of the spleen are two discrete questions, there were separate study arms for each question.

Search Strategy

Literature searches by using Medline, Embase, Cochrane Central Register of Controlled Trials, Database of Abstracts of Reviews of Effects, and Cochrane Database of Systematic Reviews were independently performed by two authors (M.D.F.M. and A.Z.K., fellowship-trained abdominal radiologists with 4 and 5 years of experience, respectively), up to July 20, 2010. No language restrictions were applied. Medical subject headings, or MeSH, and flow diagrams are outlined in Figure 1. Retrieved titles and abstracts were independently reviewed by two authors (M.D.F.M., A.Z.K.) for relevance. Full text of relevant studies was retrieved for further evaluation. Reference lists of these relevant studies were checked manually to identify other relevant articles.

Inclusion criteria for the diagnostic accuracy arm were as follows: *(a)* Image guidance (computed tomography [CT], ultrasonography [US], or fluoroscopy) was used for all cases. *(b)* The data were retrievable to calculate a 2×2 contingency table. *(c)* An acceptable reference standard (surgery, biopsy of a different organ, imaging, and/or clinical follow-up) was used for the majority of patients. *(d)* The study was not exclusively in pediatric patients. *(e)* The article was not a case report. *(f)* The study patients were not a subset of patients from another included article.

Inclusion criteria for the complication rate arm were as follows: *(a)* Image guidance (CT, US, or fluoroscopy) was used for all cases. *(b)* Complications were reported. *(c)* Biopsies were performed in inpatients, or there was a minimum of 24-hour postbiopsy follow-up for outpatients. *(d)* The study was not exclusively in pediatric patients. *(e)* The article was not a case report. *(f)* The study patients were not a subset of patients from another included article.

The rationale for *c* was that more than 25% of complications related to hemorrhage at percutaneous biopsy of the liver occurs more than 4 hours after the procedure (10,12).

Eligibility for both the diagnostic accuracy and complication rate arms was determined independently by two

Implication for Patient Care

- For cases where the spleen is the only abnormal or most accessible organ available for biopsy and a tissue diagnosis is required, the data presented in this study support the use of image-guided percutaneous biopsy of the spleen as a safe alternative to splenectomy.

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Abbreviations:
CI = confidence interval
CNB = core-needle biopsy
FNAB = fine-needle aspiration biopsy
QUADAS = Quality Assessment of Diagnostic Accuracy Studies
STROBE = Strengthening the Reporting of Observational Studies in Epidemiology

Author contributions:
Guarantors of integrity of entire study, M.D.F.M.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, all authors; clinical studies, A.Z.K., D.B.M.; statistical analysis, M.D.F.M., D.B.M.; and manuscript editing, all authors

Potential conflicts of interest are listed at the end of this article.

Figure 1

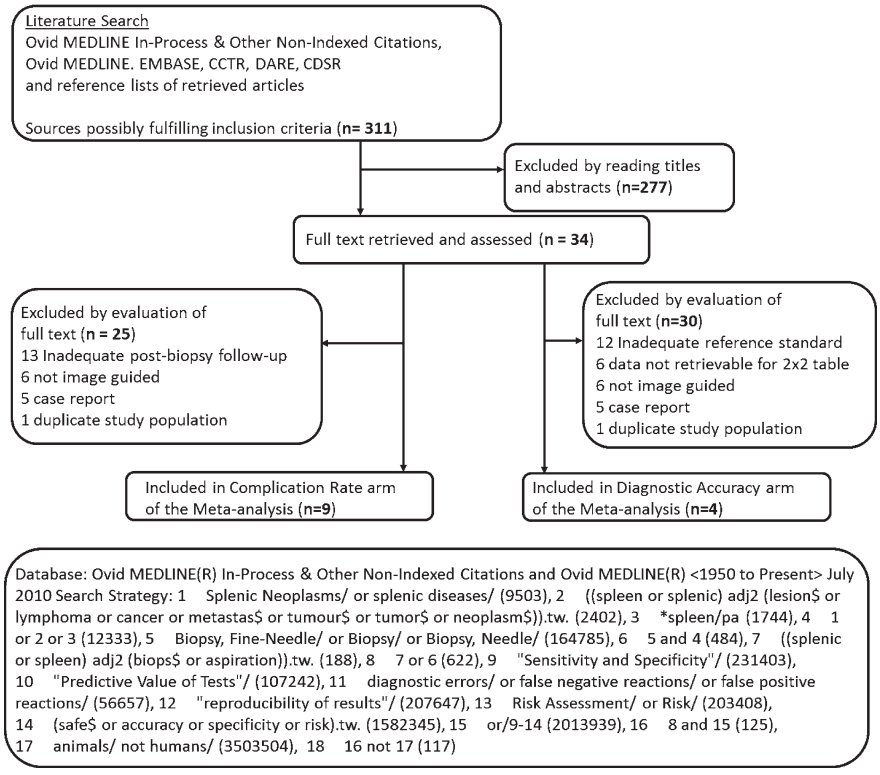

Figure 1: Study flow diagram and sample search strategy. *CCTR* = Cochrane Central Register of Controlled Trials, *CDSR* = Cochrane Database of Systematic Reviews, *DARE* = Database of Abstracts of Reviews of Effects.

reviewers (M.D.F.M., A.Z.K.), with disagreements resolved by consensus. Studies were excluded if any of the inclusion criteria were not met.

Data Extraction and Quality Assessment

Two authors (M.D.F.M., A.Z.K.) independently extracted data for the diagnostic accuracy arm by using data extraction sheets with 2 × 2 tables for each of the following: fine-needle aspiration biopsy (FNAB) and core-needle biopsy (CNB), CNB only, and FNAB only. Disagreements were resolved by consensus. The following definitions were used. A true-positive result was an index test (biopsy) result of either malignancy or infection confirmed with the reference standard. A true-negative result was an index test result of normal spleen, benign lesion, no malignancy, or no infection confirmed with the reference standard. A false-positive result was an index test result of either malignancy or infection not confirmed with the reference standard. A false-negative result was an index test result of normal spleen, benign lesion, no evidence of malignancy, or no evidence of infection with either malignancy or infection diagnosed with the reference standard. Insufficient samples were excluded from the analysis on the assumption that they occur randomly (24). Samples to which no reference standard was applied were excluded.

The methodologic quality and potential sources of bias for each study were assessed by using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) 14-item scale (24). Two authors scored independently (D.B.M., M.D.F.M.), and differences were resolved by consensus. QUADAS ratings were charted by using a review manager software program (RevMan, version 5.0, 2008; Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

Two authors (A.Z.K., M.D.F.M.) independently extracted data for the complication rate arm by using a data extraction sheet, with differences resolved by consensus (data points are the column headings in Tables 1 and 2). The complications were classified as major or minor per Society of Interventional Radiology guidelines (25). Complication rate was calculated per biopsy. A biopsy was defined as biopsy performed on two separate dates or as a CNB in addition to a FNAB performed during the same procedure. The methodologic quality and potential sources of bias for each study were assessed by using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (26). Scoring was done independently by two authors (D.B.M., M.D.F.M.), with disagreement resolved by consensus.

For both study arms, the risk for publication bias was visually assessed across studies with a funnel plot of the studies' logarithm of the diagnostic odds ratio against the standard error. In addition, asymmetry of the funnel plot was quantified with the Egger test (27).

Data Analysis

The 2 × 2 data were summarized in forest plots of sensitivity and specificity for each study. This was done for all biopsies (FNAB and CNB), CNB, and FNAB. Pooled summary of sensitivity and specificity was calculated by using the random-effects model weighted by the inverse variance (28). Complication rate for total biopsies (FNAB and CNB), FNAB, and CNB was calculated and displayed per study by using a forest plot. Sensitivity analysis was performed by removing cases with needles larger than 18 gauge; this was done because needles larger than 18 gauge are not routinely used in current practice in the spleen, as well as other intraabdominal organs, because of concerns regarding higher rates of hemorrhage (5,13,29). Pooled summary complication rate for FNAB, CNB, and total biopsies was calculated by using the random-effects model weighted by the inverse variance (28).

Heterogeneity was quantified and appropriated by using the I^2 statistic

Table 1

Summary of the Demographic and Study Design Characteristics of the Included Studies

Study	Clinical Setting	Dates	Prospective Design	Indication for Biopsy	Male-to-Female Ratio	Mean Age (y)	Study Arm*
Civardi et al (5) (2001)	Eight centers (three GI, three infectious disease, two hematology departments)	NS	No	Biopsy only performed in focal lesions with safe access away from hilum	211/187	NS	CR and DA
Gómez-Rubio et al (16) (2009)	Five GI departments	1992–2007	No	Biopsy if firm diagnosis not possible from clinical or imaging studies	26/26	52	CR and DA
Liang et al (29) (2007)	Single center	1998–2005	Yes	Diagnosis not possible from imaging (seven pain or fever, six? lymphoma, one? metastasis, one weight loss)	29/13	NS	CR and DA
Cavanna et al (32) (1992)	Single center	NS	No	Lymphoma patients (11 Hodgkin, 35 NHL), five diagnostic, 32 staging, seven restaging, two follow-up	23/23	NS	CR
Di Stasi et al (33) (1996)	Single center	1982–1995	No	46 focal lesions NYD, 114 lymphoma staging in clinical trial	NS	NS	CR
Keogan et al (14) (1999)	Single center	1995–1997	No	Five? metastasis, two? lymphoma, three immuno-compromised, five incidental lesion, two anemia, one IV drug use	3/15	55	CR
Lindgren et al (15) (1985)	Single center (medicine and oncology departments)	1983–1984	No	24 lymphoma (19 staging, five restaging), five B symptoms, one splenomegaly, two severe hypercalcemia	20/12	38	CR
Suzuki et al (34) (1987)	Single center	NS	No	Staging of disease in eight patients with NHL	7/1	52	CR
Venkaramu et al (35) (1999)	Single center	1993–1998	No	23 fever, six hematologic malignancy and fever, two anemia or fever, two? lymphoma, two incidental lesion	28/7	NS	CR
Tam et al (6) (2008)	Tertiary cancer center	1992–2007	No	101? recurrent lymphoma, 39? metastasis, 16 unknown diagnosis	78/69	54.9	DA

Note.—GI = gastrointestinal, IV = intravenous, NHL = non-Hodgkin lymphoma, NS = not specified, NYD = not yet diagnosed, ? = query.

* CR = complication rate, DA = diagnostic accuracy.

(30). Heterogeneity was classified as not likely contributory (I^2 = 0%–40%), moderate (I^2 = 30%–60%), substantial (I^2 = 50%–90%), or considerable (I^2 > 75%) (31).

All statistical analyses were conducted with software (Comprehensive Meta-Analysis, version 2.2; Biostat, Englewood, NJ).

Results

The literature search identified 311 articles. Sample search strategy and study flow diagram are provided in Figure 1. After screening the titles and abstracts, 277 articles were excluded because one or more inclusion criteria were not met. Full text of the remaining 34 articles was retrieved and evaluated. Of these, 25 were excluded from the complication rate arm of the study, while 30 were excluded from the diagnostic accuracy arm of the study for reasons specified in Figure 1. Nine studies were included in the complication rate arm of the study (5,14–16,29,32–35), and four studies were included in the diagnostic accuracy arm of the study (5,6,16,29). Personal communication with the author confirmed that one study contained a subset of patients from another article (5,36) (Luigi Cavanna, MD, personal communication, July 2010). Table 1 summarizes the demographic and study design characteristics of the included studies.

Complication Rate Arm

Table 2 summarizes each included study. Eight hundred fifty-nine biopsies were performed in 741 patients. Three hundred seventy CNBs and 489 FNABs were performed. CNB needle size ranged from 14 to 22 gauge. FNAB needle size ranged from 20 to 25 gauge.

A forest plot with pooled total complication rates for all biopsies (FNAB and CNB), FNAB only, and CNB only is

Table 2

Summary Characteristics and Data from the Included Studies in the Complication Rate Arm

Study	Prebiopsy Work-up	Postbiopsy Follow-up	No. of Biopsies*	Needles Used	Average No. of Passes†	Major Complications Description*	Minor Complications Description*	No. of Splenectomies‡	STROBE Score§
Civardi et al (5) (2001)	INR < 1.6, platelet count > 70 000/μL	All inpatients	453 (298/155)	FNAB: 22-gauge Chiba, CNB: 20–21-gauge Surecut	1.6 (1–4)	Three: two hemorrhages requiring transfusion, one pneumothorax requiring chest tube (1/2)	18: 13 pain, two subcapsular hematomas, two small hemoperitoneum, one vasovagal episode (14/4)	0	17
Gómez-Rubio et al (16) (2009)	Platelet count > 60 000/μL, PT > 50%, normal PTT	24 hr inpatient monitoring	62 (25/37)	FNAB: 22 gauge (17), 20 gauge (16), 25 gauge (4), CNB: 19.5 gauge (20), 18 gauge (3), 14 gauge (1)‖	1.4 (1–4)	One hemorrhage requiring splenectomy, 19.5-gauge CNB, no coagulopathy (0/1)	One subcapsular hematoma, 18-gauge CNB (0/1)	1 (19.5-gauge CNB)	16
Liang et al (29) (2007)	Platelet count > 100 000/μL, PTT < 20 sec, PT > 50%	2 hr US and 1 mo clinical, CT and US follow-up	43 (17/26)	FNAB: 21 gauge, CNB: 18 gauge	2.3 CNB, 2.8 FNAB (NS)	One hemorrhage requiring transfusion, 18 gauge (0/1)	0	0	19
Cavanna et al (32) (1992)	Platelet count > 70 000/μL, PTT normal, PT > 50%	24 hr US and CBC, plus US 1 and 2 wk	46 (0/46)	CNB: 21–22-gauge Surecut	1.4 (1–3)	0	0	0	13
Di Stasi et al (33) (1996)	Platelet count > 70 000/μL, PTT < 40 sec, PT > 50%	24 hr US and CBC	160 (95/65)	FNAB: 22-gauge Chiba, CNB: 21-gauge Surecut	<4 (NS)	0	One subcapsular hemotoma, 21-gauge CNB (0/1)	0	14
Keogan et al (14) (1999)	Platelet count > 150 000/μL, PTT 20–33 sec, PT 11.3–13.3 sec	4 hr monitor and 48 hr phone call	20 (19/1)	FNAB: 22 gauge, CNB:18 and 20 gauge	NS (1–4)	0	0	0	14
Lindgren et al (15) (1985)	Normal except two patients with low platelet count 40 000–50 000/μL (transfusion prior to biopsy)	4 hr ICU then 20 hr inpatient	32 (0/32)	CNB: 14-gauge Tru-cut	NS (1–3)	Four: three hemorrhages requiring transfusion at 3, 6, and 8 hr, one hemorrhage at 24 hr requiring splenectomy (0/4)	16: all slight to moderate shoulder pain (0/16)	1 (14-gauge CNB)	14
Suzuki et al (34) (1987)	PT, PTT, CBC, platelet count checked	24 hr follow-up US and CBC	8 (0/8)	CNB: 21-gauge Surecut (through 18-gauge guide)	NS	0	0	0	13
Venkaramu et al (35) (1999)	Clotting factors checked and corrected where necessary	24–48 hr inpatient monitoring	35 (35/0)	FNAB: 22 gauge spinal	NS	One hemorrhage requiring transfusion, 22 gauge (1/0)	0	0	17

Note.—CBC = complete blood count, ICU = intensive care unit, INR = international normalized ratio, NS = not specified, PT = prothrombin time, PTT = partial thromboplastin time.

* Data in parentheses are FNAB-to-CNB ratios.

† Data in parentheses are ranges.

‡ Data in parentheses are needle types.

§ STROBE score is out of 22.

‖ Data in parentheses are number of biopsies.

Figure 2

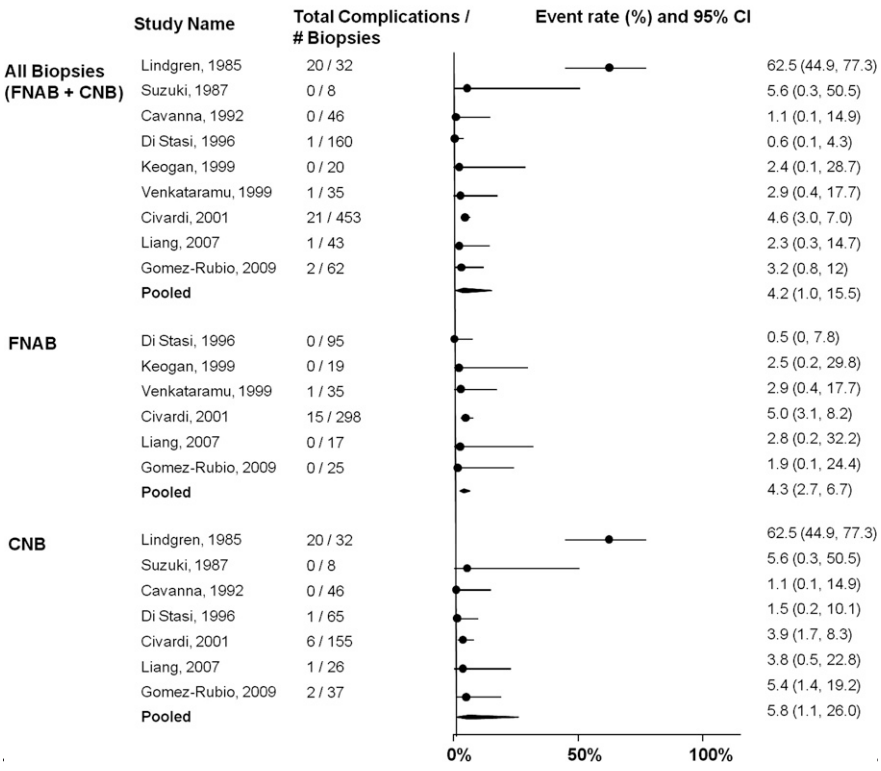

Figure 2: Forest plot with pooled total (major and minor) complication rates.

Figure 3

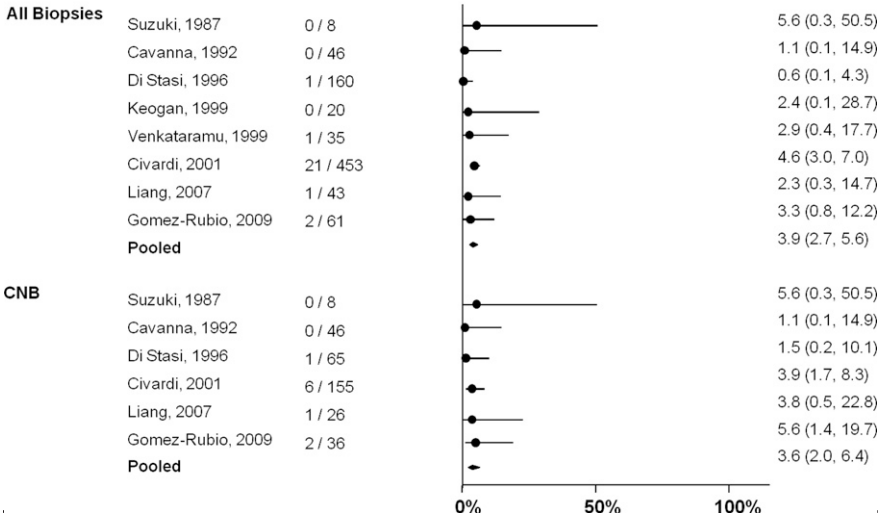

Figure 3: Forest plot of total (major and minor) complication rate sensitivity analysis (needles larger than 18 gauge removed) with pooled rates. FNAB was not included because rates were unchanged from Figure 2.

summarized in Figure 2. Complications were reported in 46 of 859 biopsies (10 major and 36 minor). Of the 10 major complications, nine were related to hemorrhage and one was pneumothorax. Two cases of splenectomy for treatment of postbiopsy hemorrhage were reported—one after a 14-gauge CNB (15) and another after a 19.5-gauge CNB (16). No deaths were reported. Of the 36 minor complications, 29 were related to pain, six were related to hemorrhage, and one was a vasovagal episode. Complications are listed in Table 2. Eight major and 22 minor complications were reported for 370 CNBs. Two major and 14 minor complications were reported for 489 FNABs. The major complication rate was 2.2% (95% confidence interval [CI]: 0.8%, 5.6%) for all biopsies, 1.3% (95% CI: 0.5%, 3.3%) for FNAB, and 3.2% (95% CI: 1.3%, 7.9%) for CNB.

A forest plot with pooled total complication rates for sensitivity analysis is summarized in Figure 3. FNAB complication rate was unchanged because all FNABs were performed with needles smaller than 18 gauge. Sensitivity analysis with the removal of 33 biopsies performed with needles larger than 18 gauge demonstrated six major and 20 minor complications reported in 826 biopsies. This sensitivity analysis demonstrated a major complication rate of 1.3% (95% CI: 0.6%, 2.5%) for all biopsies and 1.9% (95% CI: 0.8%, 4.4%) for CNB. Among the 33 biopsies performed with needles larger than 18 gauge (all 14 gauge), four major and 16 minor complications were reported; these included one splenectomy to treat hemorrhage (15,16). For these biopsies performed with 14-gauge needles, the pooled major complication rate was 12.5% (95% CI: 4.8%, 28.9%), and the pooled total complication rate was 60.6% (95% CI: 43.4%, 75.6%).

The assessment of potential publication bias by using visual assessment of funnel plot and the Egger test demonstrated no asymmetry of the funnel plot; thus, publication bias was not suspected. The between-study heterogeneity was considerable (I^2 = 90.8%, P = <.0001). However, when the cases with needles

Table 3

Summarized Data from the Included Studies in the Diagnostic Accuracy Arm

Study	No. of True-Positive Findings	No. of False-Negative Findings	No. of True-Negative Findings	No. of False-Positive Findings	No. of Excluded Cases	Reference Standard
Civardi et al (5) (2001)	112	12	250	2	22 (insufficient samples)	45 surgical biopsy of the spleen, 26 splenectomy, seven autopsy, 320 clinical and imaging follow-up > 6 mo
Gómez-Rubio et al (16) (2009)	49	7	6	0	0	Surgical pathologic findings, therapy response, clinical and imaging follow-up > 2 yr (not specified for each)
Liang et al (29) (2007)	19	3	17	3	0	27 surgical pathologic findings, 11 therapy response, four clinical and imaging follow-up > 6 mo
Tam et al (6) (2008)*	84	22	32	0	18 (12 insufficient samples, six no reference standard)	31 splenectomy or 52 biopsy of other organ < 3 mo; 15 biopsy other organ <1 yr; 44 clinical and imaging follow-up 2 wk–14 yr; six lost to follow-up

* For Tam et al, there were 156 biopsies, of which 131 were FNABs, 13 were CNBs, and 12 were unknown. For FNAB, 22–23-gauge needles were used. For CNB, 18–20-gauge needles were used. The average number of passes was 2.8, with a range of one to six. This information is in Table 2 for the other three studies.

larger than 18-gauge were removed in the sensitivity analysis, the heterogeneity was not likely contributory ($I^2 = 0$, $P = .59$).

STROBE methodologic quality score for each study is listed in Table 2. The mean score for the nine included studies was 15.2 of 22 (95% CI: 13.6, 16.8). The median was 14, and the range was 13–19. Areas of deficiency varied between studies, with no consistent areas of deficiency identified.

Diagnostic Accuracy Arm

Table 3 summarizes each included study. A total of 714 biopsies (FNAB and CNB) were performed in 639 patients. The 34 biopsies with insufficient samples were excluded from analysis (22 for Civardi et al and 12 for Tam et al) (5,6). Six biopsies to which no reference standard was applied were also excluded from the analysis (6). In the initial article by Tam et al, five biopsies were initially classified as having false-positive findings, but should have been classified as having false-negative findings (Alda Tam, MD, personal communication, July 2010). Reference standard applied and 2 × 2 table data are summarized in Table 3.

Figure 4

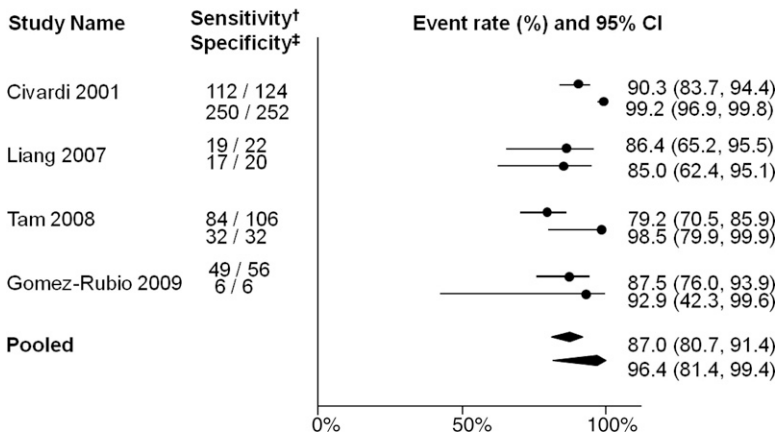

Figure 4: Forest plot with pooled sensitivity and specificity for all biopsies (FNAB and CNB). † = No. of true-positive findings/(no. of true-positive findings + no. of false-negative findings). ‡ = No. of true-negative findings/(no. of true-negative findings + no. of false-positive findings).

A forest plot of sensitivity and specificity for all biopsies (FNAB and CNB) with pooled result is demonstrated in Figure 4. The pooled sensitivity was 87.0%, with I^2 of 47.6% (moderate heterogeneity), and specificity was 96.4%, with I^2 of 73.6% (substantial heterogeneity) for all biopsies (FNAB and CNB). Pooled rates for CNB only were calculated from the studies for which core biopsy 2 × 2 data were retrievable (5,16,29): Sensitivity was 86.8% (95% CI: 78.2%, 92.4%), with I^2 of 0% (not likely contributory), and specificity was 96.8% (95% CI: 90.4%, 99.0%), with I^2 of 0% (not likely contributory). Pooled rates for FNAB only were calculated from the studies for which 2 × 2 data were retrievable (5,16,29): Sensitivity was 84.1% (95% CI: 77.0%, 89.3%),

Figure 5

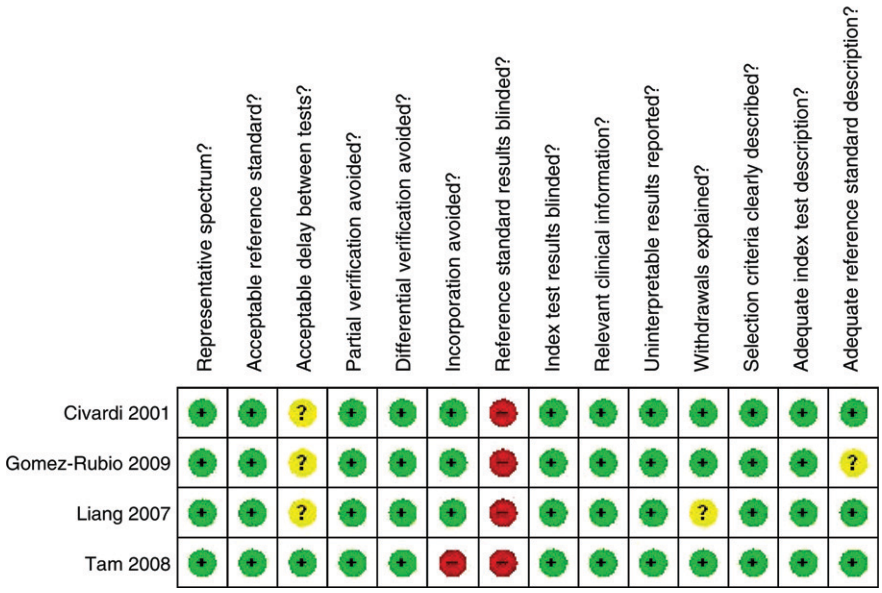

Figure 5: Chart of study quality assessment with QUADAS checklist for the studies included in the diagnostic accuracy arm. Green circle = yes. Red circle = no. Yellow circle = unclear.

with I^2 of 0% (not likely contributory), and specificity was 92.5% (95% CI: 35.6%, 89.4%), with I^2 of 85.7% (considerable heterogeneity).

The assessment of potential publication bias by using visual assessment of funnel plot and the Egger test was not performed, because, with only four included studies, it was not thought to be a useful test (27).

Assessment of methodologic quality of included articles according to the 14 QUADAS criteria is demonstrated in Figure 5. Nine of the 14 criteria were met by all studies. Three of four studies were unclear in that they did not specify the length of delay between the index test and the reference standard. None of the studies had the reference standard results blinded to the results of the index test. One study incorporated the index test as part of the reference standard for six of the 138 cases; these cases were excluded from the analysis (6). One study, a randomized control trial, did not specify if there were any withdrawals or refusals to participate (29). One study did not have a sufficient description of the reference standard in that it did not specify exactly which reference standard was applied to each case (16).

Discussion

This meta-analysis showed an overall complication rate for splenic biopsy of 4.2% for all biopsies and a slightly higher rate for CNB (5.8%) than for FNAB (4.3%). The major complication rates were 2.2% for all biopsies, 3.2% for CNB, and 1.3% for FNAB. Nine of the 10 major complications were related to hemorrhage; the other was a pneumothorax. Splenectomy was required to treat hemorrhage in two cases; there were no deaths. When needles larger than 18 gauge (which are not routinely used in current practice) were removed from the analysis, the complication rates were considerably lower: total complication rate was 3.9% for all biopsies and 3.6% for CNB; the major complication rate was 1.3% for all biopsies and 1.9% for CNB. The fact that heterogeneity was considerable when all biopsies were included, but was not likely contributory when biopsies performed with needles larger than 18 gauge were removed, underscores the effect of these larger needle biopsies on the complication rate. This heterogeneity is visually evident in Figure 2; the Lindgren et al study, which used only large (14-gauge) needles, was a clear outlier with a much higher complication rate.

These complication rates reflecting the current standard of practice with smaller needles are comparable to those published for other abdominal organs such as the liver and kidney. The major complication rates reported are 0.5%–3.3% for liver biopsy and 0.7%–6.3% for kidney biopsy (10). They are also lower than the reported complication rates associated with the most likely alternate procedure—splenectomy with associated morbidity (8.6%–37%) and mortality (0%–2.9%) rates (7–9).

This meta-analysis showed a high overall diagnostic accuracy for image-guided percutaneous biopsy of the spleen. For all biopsies (FNAB and CNB), sensitivity was 87.0% and specificity was 96.4%. The diagnostic accuracy is likely lower than what could be obtained with splenectomy. However, given the lower complication rate of biopsy, the trade-off is acceptable. Although the pooled sensitivity and specificity for CNB and FNAB were similar, the heterogeneity is considerable for specificity in the FNAB group compared with not likely contributory in the CNB group. This may be related to the difficulty in diagnosing lymphoma by using FNAB, which is a common indication for splenic biopsy.

It would have been interesting to know if the complication rate differed for focal versus infiltrative processes; however, this data were not retrievable from the included studies. In addition, data could not be retrieved to determine whether the size of the spleen undergoing biopsy affected the complication rate.

Our review was limited by the relatively low number of studies that met the inclusion criteria; this was most pronounced in the diagnostic accuracy arm. The strict inclusion criteria may have contributed to this low number of studies. The strict inclusion criteria were thought to be necessary to ensure that the study quality was high enough to have data from which meaningful conclusions

could be drawn. The composite reference standard used in the studies is not as optimal as surgical pathologic findings; however, it would not be either practical or ethical to obtain splenectomy specimens in most cases. Thus, the composite reference standard is the best available.

The exclusion of 34 insufficient samples on the basis of the assumption that they occur at random is potentially flawed. False-negative results may be overrepresented in the insufficient samples, leading to overestimation of diagnostic accuracy. Furthermore, smaller needles may lead to a higher rate of insufficient samples; thus, exclusion of these samples may artificially increase the diagnostic accuracy for smaller needles.

The complication rate may have been underestimated for two reasons. A 24-hour postbiopsy follow-up may not have captured all complications. In other organs such as the liver and kidney, up to 20% of major bleeding complications occur more than 24 hours after the biopsy (10). The patients enrolled in the studies do not represent a truly consecutive sample of patients. Most studies specified that only biopsies that were safe and/or indicated were performed. Thus, the subset of patients who underwent biopsy in this study likely would have a lower complication rate than a consecutive sample of patients referred for biopsy who were not screened for safety prior to biopsy.

The search of the literature may have been less than complete, because sources such as abstracts presented at conferences and unpublished studies were not included in the search strategy.

The current common practice of reserving biopsy of the spleen for cases when no other organ is available for biopsy is reasonable because other organs such as superficial lymph nodes may have lower associated complication rates. In addition, the physician performing the biopsy may have more experience and comfort with biopsy of organs such as the liver. For cases where the spleen is the only abnormal or most accessible organ for biopsy and a tissue diagnosis is required, the data presented in this study support the use of image-guided percutaneous biopsy of the spleen as a safe alternative to splenectomy, with a high overall diagnostic accuracy.

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