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Anal Lymphogranuloma Venereum Infection Screening With IgA Anti-Chlamydia trachomatis-Specific Major Outer Membrane Protein Serology

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Background: Anal lymphogranuloma venereum (LGV) infections, caused by Chlamydia trachomatis biovar L (Ct+/LGV+), are endemic among men who have sex with men (MSM). Anal non-LGV biovar Ct infections (Ct+/LGV−) can be eradicated with 1 week doxycycline, whereas Ct+/LGV+ infections require 3-week doxycycline. To differentiate Ct+/LGV+ from Ct+/LGV− infections, biovar-specific Nucleic Acid Amplification Test (NAAT) are standard, but also expensive and laborious. A chlamydia-specific serological assay could serve as an alternative test.

Methods: MSM were screened for anal Ct+/LGV+ and Ct+/LGV− infections with a commercial nonspecific NAAT and an in house biovar L-specific NAAT. Serum samples were evaluated with chlamydia-specific anti-Major Outer Membrane Protein (MOMP) and antipiloplyosaacaride assays of IgA and IgG classes. Asymptomatic patients were identified as: (1) no anal complaints or (2) no microscopic inflammation (i.e., <10 leucocytes per high power field in anal smears).

The best differentiating assay was subsequently evaluated in 100 Ct+/LGV+ and 100 Ct+/LGV− MSM using different cut-off points.

Results: The anti-MOMP IgA assay was the most accurate to differentiate Ct+/LGV+ (n = 42) from Ct+/LGV− (n = 19) with 85.7% sensitivity (95% confidence interval [CI], 72.2–93.3) and 84.2% specificity (95% CI, 62.4–94.5), even among asymptomatic patients. In a population comprising 98 Ct+/LGV+ and 105 Ct+/LGV− patients, the anti-MOMP IgA assay scored most accurate when the cut-off point was set to 2.0 with 75.5% (95% CI, 65.8–83.6) sensitivity and 74.3% (95% CI, 64.8–82.3) specificity.

Conclusions: The IgA anti-MOMP assay can identify a considerable proportion of the (asymptomatic) anal LGV infections correctly. Yet, biovar L-specific NAAT are still the preferred diagnostic tests in clinical settings.

Lymphogranuloma venereum (LGV) is an invasive ulcerative sexually transmitted infection (STI) caused by Chlamydia trachomatis biovar L.1 The infection spreads beyond mucosal linings into connective tissue layers and through lymphatic vessels and causes destructive and systemic inflammatory reactions with extensive pathogen specific antibody production. Acute anal LGV infections are characterized by anal cramps, pain, bloody discharge, and constipation. If left untreated, chronic disease can lead to irreversible anal strictures causing soiling, pain, constipation, and mega colon.2 In contrast, anal C. trachomatis infections caused by biovars D-K do not spread beyond the mucosa and generally cause far less symptoms as well as usually minimal antibody production.

Since 2003 an ongoing epidemic of anal LGV infections among men who have sex with men (MSM) was first reported in the Netherlands, followed by other Western countries.3 Anal LGV infections are associated with high risk behavior reflected in numerous coinfections like HIV, syphilis, hepatitis C, hepatitis B, and with the use of rectal enemas (douching).4–6

Routine screening of MSM with receptive anal contact on anal C. trachomatis infections is recommended in the United States Centers for Disease Control and Prevention and in the European IUSTI/World Health Organization guidelines.7,8 Sequenalt LGV serovar confirmation is desirable as anal LGV infections require doxycycline for 21 days, whereas 7 days suffice for anal non-LGV (biovars D-K) chlamydia infections.9

In contrast to textbook reports, a considerable portion of the anal LGV infections in the current epidemic are asymptomatic (i.e., without patient-reported complaints or without clinical signs) at the time of diagnosis. In a previous retrospective study we showed that, on anoscopy examination, mucosal membrane abnormalities were visible in only 47% of 87 cases with an anal LGV infection, and that signs of microscopic inflammation (i.e., >10 leucocytes counted in a high power field in a Gram-stained rectal smear) were present in 61%.7 In
a prospective study including 32 cases with an anal LGV infection, only 44% reported anal complaints. The cause of an asymptomatic presentation is unknown but is possibly related to an altered immune response because of concurrent HIV infection (which is present in approximately 80% of the cases). Some national guidelines recommend LGV screening only in cases with suspected symptoms. Consequently, asymptomatic infections will be missed.

The gold standard to diagnose anal LGV infections nowadays is the detection of LGV biovar-specific chlamydia DNA through “in house” developed nucleic acid amplified tests, but these tests are expensive and require specialized laboratory conditions. There is a need for less expensive, less laborious, and less specialized screening methods to screen large patient groups at risk for LGV. Serological tests that detect antibodies against Chlamydia-specific membrane proteins could be an option for this purpose, but ideally these assays should also detect asymptomatic infections. In this study, we evaluated the diagnostic characteristics of 4 chlamydia-specific serological assays to detect anal LGV. The study population consisted of MSM visiting the STI clinic with a confirmed anal chlamydia infection.

**MATERIALS AND METHODS**

**Routine Anal Infection Screening Procedure**

At the time of this study, all MSM reporting receptive anal sex in the preceding 6 months at the Amsterdam STI outpatient clinic were routinely checked for anal chlamydia (including LGV) and gonorrhoea infections by collection of mucosal swabs during anoscopy as described earlier. The following anal complaints were recorded: discharge, pain or itch, and constipation or a sense of incomplete defecation. Upon anoscopy the following mucous membrane abnormalities were recorded: discharge, edema, tissue fragility (bloody mucosal surfaces when swabs were obtained), ulceration, and abscesses. Moreover, the number of leucocytes per high power field (leucos/hpf) were counted in Gram-stained anal mucosal smears. Patients were considered to have a symptomatic proctitis if they had anal complaints or mucous membrane abnormalities, and ≥10 leucos/hpf. Symptomatic patients started a presumptive treatment of doxycycline 100 mg orally b.i.d. till the chlamydia nucleic acid test results became available. Moreover, if Gram-negative diplococci in leucocytes were noticed in the anal smear, suggestive for anal gonorrhoea, a presumptive treatment of ceftriaxone 500 mg intramuscularly once was administered. During anoscopic examination, swabs for chlamydia nucleic acid identification (Cobas Amplicor; Hoffman-La Roche) and gonorrhoea cultivation were obtained from all patients. On all Chlamydia-positive (CT+) anal samples, additional biovar L confirmation was performed with a nucleic acid test, as described earlier. The chlamydia test results were available within 7 days, and the biovar L confirmation within 10 to 13 days after the initial screening visit.

**Serologic Test Evaluation Upon Time of Diagnosis**

For this part of the analysis we did not use any additional data or samples other than obtained in the routine screening procedure of the clinic. Therefore, neither additional ethical approval, nor additional patient consent was considered necessary.

To evaluate the different Chlamydia-specific serologic assays, we compared patients with anal LGV infections (CT+ / LGV+ i.e., an anal swab positive for chlamydia L biovar) to patients with anal non-LGV chlamydia infections (CT+ / LGV− i.e., an anal swab positive for Chlamydia non-L biovar). In a subanalysis, the 4 assays were evaluated according to patient reported anal complaints (discharge, pain, itch, constipation, or a sense of incomplete defecation) and to microscopic signs of inflammation (<10 leucos/hpf in the anal smear).

**Serodynamic Evaluation After Treatment of Anal Infections**

For the evaluation of chlamydia humoral antibody dynamics after doxycycline therapy, a selection of participants with CT+/LGV+ and CT+/LGV− was followed up during 1 year. This part of the study was in accordance with the Helsinki Declaration, and we obtained ethical approval from the Academic Medical Centre ethical committee, Amsterdam, The Netherlands.

Consent to participate in the study was obtained from patients with a symptomatic proctitis during the initial screening visit. Asymptomatic patients were asked for consent when they returned for doxycycline therapy of their anal chlamydia infection. Patients with CT+/LGV+ were instructed to use 100 mg of doxycycline twice daily for a minimum duration of 21 days. Patients with CT+/LGV− were treated for a minimum of 7 days with doxycycline 100 mg twice daily. Serum was collected on the day doxycycline treatment was commenced (t0) and at subsequent visits during Weeks 1, 2, 3, 6, 12, 24, 36, and 52. Patients with the most complete set of serum samples during the follow-up period were selected and used to perform the assays on.

**Chlamydia-Specific Serologic Tests**

Serologic assays for IgA anti-major outer membrane protein (MOMP) (C. trachomatis-IgA-pELISA medac, Hamburg, Germany), IgG anti-MOMP (C. trachomatis-IgG-pELISA medac), IgA anti-LPS (Chlamydiens-IgA-ELISA medac), and IgG anti-LPS (Chlamydiens-IgG-ELISA medac) were performed on serum samples in microtiter plate wells according to the manufacturer’s guidelines. The test results were given as optical density, calibrated to a positive and negative control sample per microtiter plate and expressed as cut-off index (COI) per sample.

For the IgA anti-MOMP and IgG anti-MOMP assays (and according to the manufacturer’s guidelines) a negative cut-off titer corresponded with COI <0.9, an equivocal titer with COI ≥0.9 but ≤1.1 and a positive titer with COI >1.1. In the test evaluation, negative and equivocal titers were considered not indicative for LGV proctitis. For the IgA anti-LPS and IgG anti-LPS assay titers <1:200 were considered not indicative for LGV proctitis. For the IgA anti-LPS this corresponded to a COI <3.61 and for the IgG anti-LPS assay to a COI <1.81.

**Statistical Analysis**

Per assay at t0, sensitivity, specificity, and the diagnostic odds ratio were calculated with 95% confidence intervals (95% CI) to differentiate CT+/LGV+ from CT+/LGV−. Comparing the performance of competing tests with paired indicators such as sensitivity and specificity can have a disadvantage, especially, if one test does not outperform the other on both indicators. The diagnostic odds ratio is the equivalent of (true positives/false negatives)/(false positives/true negatives). As a single indicator of diagnostic performance, it overcomes the disadvantage of paired indicators and allows the comparison of various diagnostic tests for one indication. A value of 1 indicates that a test does not discriminate between patients with the disorder and those without it.

The 4 assays were then evaluated about symptoms (i.e., patient reported complaints and leucos/hpf). Data were presented
TABLE 1. Test Characteristics of 4 Chlamydia Specific Serological Assays to Differentiate Anal LGV Infections From Non-LGV Chlamydia Anal Infections in 61 Men Who Have Sex With Men, Amsterdam STI Outpatient Clinic

<table>
<thead>
<tr>
<th>Test</th>
<th>Cut-off Titer</th>
<th>Ct+/LGV+</th>
<th>Ct+/LGV−</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Diagnostic Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA anti-MOMP</td>
<td>Neg/equiv</td>
<td>6</td>
<td>16</td>
<td>85.7 (72.2–93.3)</td>
<td>84.2 (62.4–94.5)</td>
<td>32.0 (7.1–144.3)</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>36</td>
<td>3</td>
<td>92.9 (81.0–97.5)</td>
<td>31.6 (15.4–54.0)</td>
<td>6.0 (1.3–27.5)</td>
</tr>
<tr>
<td>IgG anti-MOMP</td>
<td>Neg/equiv</td>
<td>3</td>
<td>6</td>
<td>9.3 (81.0–97.5)</td>
<td>31.6 (15.4–54.0)</td>
<td>6.0 (1.3–27.5)</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>39</td>
<td>13</td>
<td>47.6 (33.4–62.3)</td>
<td>94.7 (75.4–99.7)</td>
<td>16.4 (2.0–134.0)</td>
</tr>
<tr>
<td>IgA anti-LPS</td>
<td>&lt;1:200</td>
<td>22</td>
<td>18</td>
<td>90.5 (77.9–96.2)</td>
<td>31.6 (15.4–54.0)</td>
<td>4.4 (1.1–18.0)</td>
</tr>
<tr>
<td></td>
<td>≥1:200</td>
<td>20</td>
<td>1</td>
<td>47.6 (33.4–62.3)</td>
<td>94.7 (75.4–99.7)</td>
<td>16.4 (2.0–134.0)</td>
</tr>
</tbody>
</table>

The assays were performed on 42 patients with an anal LGV infection and 19 patients with an anal non-L biovar chlamydia infection. MOMP indicates major outer membrane protein; LPS, lipopolysaccharide; Ct+/LGV+, anal LGV biovar specific chlamydia infection; Ct+/LGV−, anal non-LGV biovar chlamydia infection; 95% CI, 95% confidence intervals.

as mean COI with 95% CI. A Student $t$ test was used and a $P$ <0.01 was considered significant. Moreover, the 4 assays were analyzed in time during the 1-year follow-up after treatment. Intraindividual correlation was accounted for in a random effects model. For this analysis the R statistical package was used.\textsuperscript{14} Data were presented as fitted mean COI trends with 95% CI.

All 4 assays were first evaluated in a limited number of patients. The test with the highest diagnostic odds ratio was then evaluated on an expanded serum panel of the last retrospective 100 MSM diagnosed with Ct+/LGV+ and 100 with Ct+/LGV− starting from June 26, 2009. Based on the results of the expanded serum panel, a continuous sensitivity, specificity, and ROC analysis was performed to determine the optimal cut-off point to differentiate between Ct+/LGV+ and Ct+/LGV− infections.

**RESULTS**

**Serologic Test Performance to Diagnose Anal LGV Infections**

The first evaluation of the 4 assays was performed in 61 MSM diagnosed with an anal chlamydia infection (42 had Ct+/LGV+, and 19 had Ct+/LGV−) in the period between August 2004 and April 2006 with oversampling of patients with an anal LGV infection for whom the inclusion period was extended until January 2008.

Overall, the IgA anti-MOMP assay had the most optimal test characteristics to differentiate Ct+/LGV+ from Ct+/ LGV− with 85.7% sensitivity (95% CI, 72.2–93.3%), 84.2% specificity (95% CI, 62.4–94.5%), and a diagnostic odds ratio of 32.0 (95% CI, 7.1–144.3) (Table 1). The other 3 assays performed worse. The IgG anti-MOMP and IgG anti-LPS lacked specificity (both 31.6% with 95% CI, 15.4–54.0) and the IgA anti-LPS lacked sensitivity with 47.6% (95% CI, 33.4–62.3).

**Performance of the Serologic Assays in Asymptomatic Patients**

In a subanalysis the 4 assays were evaluated in asymptomatic patients. The population consisted of 38 patients without anal complaints (23 with Ct+/LGV+ and 15 with Ct+/LGV−) and 22 patients with <10 leucocytes/hpf in anal smears (14 Ct+/LGV+ and 8 Ct+/LGV−). Again, the IgA anti-MOMP identified Ct+/LGV+ cases best of all 4 assays in the group reporting no complaints. The mean COI of cases reporting no anal complaints with Ct+/LGV+ was 3.7 (95% CI, 2.3–5.5) and in cases with Ct+/LGV−0.6 (95% CI, 0.4– 0.9; Fig. 1). In cases with <10 leucocytes/hpf in anal smears, only the IgA anti-MOMP assay showed significant COI differences between Ct+/LGV+ and Ct+/LGV− cases: 5.0 (95% CI, 3.3–6.8) and 1.4 (95% CI, 0.6–2.4), respectively.

In cases without complaints, the IgA anti-MOMP assay showed 73.9% sensitivity (95% CI, 53.5%–87.5%), 93.3% specificity (95% CI, 70.2%–99.7%), and a diagnostic odds ratio of 39.7 (95% CI, 4.3–369.7). In cases with <10 leucocytes/hpf in anal smears, the IgA anti-MOMP assay showed 85.7% (95% CI, 60.1%–96.0%), 75.0% (95% CI, 40.9%–92.9%), and 18.0 (95% CI, 2.0–161.1; Table 2), respectively.

**Serodynamics After Treatment**

For the serodynamic analysis, 20 patients with Ct+/ LGV+ were selected (based on the maximal number of follow-up sera) and all 19 patients with Ct+/LGV− were selected. With all 4 assays, a consistent significant downward trend in the serologic response was observed in the Ct+/LGV+ group (Fig. 2). The IgA anti-MOMP assay showed the largest decrease in the serologic titers 1 year after treatment. However, with all assays the mean COI values remained above the cut-off titer that was considered positive for an anal LGV infection.

**Performance of the IgA Anti MOMP Assay in the Expanded Serum Panel**

In a small number of individuals (n = 61), the IgA anti-MOMP assay performed best in differentiating Ct+/ LGV+ from Ct+/LGV−. We therefore evaluated this assay in a panel of 203 serum samples from successive MSM with either Ct+/LGV+ (n = 98) or Ct+/LGV− (n = 105) who visited our STI outpatient clinic in the period between January 2008 and July 2009. The area under the curve was 80.2. Sensitivity and specificity were calculated for a continuous range of cut-off points from 0 to 12 COI (Fig. 3). At the COI considered positive by the manufacturer (positive if >1.1), the specificity was 78.6 (95% CI, 69.1–86.2), the specificity 61.0 (95% CI, 51.0–70.3), and the diagnostic odds ratio 5.7 (95% CI, 3.1–10.7, Table 3). Based on the diagnostic odds ratio, the optimal cut-off point was found if the COI was considered positive >2.0 with a sensitivity of 75.5 (95% CI, 65.8–83.6), a specificity of 74.3% (95% CI, 64.8–82.3), a positive predictive value of 73.3 (63.5–81.6), a negative predictive

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value of 76.5 (67.0–84.3), and a diagnostic odds ratio of 8.9 (95% CI, 4.7–16.8).

**DISCUSSION**

**The Potential Role of IgA Anti-MOMP Assay in LGV Screening**

In a population of patients with a NAAT-proven rectal chlamydia infection, the IgA anti-MOMP assay detected LGV proctitis cases with a sensitivity, specificity, negative and positive predictive value of all around 75% (Table 3). These test characteristics make this assay unsuitable for diagnostic purposes and it cannot replace a *C. trachomatis* biovar-specific NAAT in a clinical setting.

However, the number of LGV cases among MSM is still increasing.3,15 Recent reports of endemically acquired LGV among heterosexual patients in Spain and Portugal could herald transmission outside the initial core groups and needs close monitoring.16,17 An IgA anti-MOMP assay could serve as a cost-effective marker to screen large populations

**Figure 1.** Mean serology cut-off indices with 4 chlamydia specific serological assays, Amsterdam STI outpatient clinic. The assays were performed on 42 patients with an anal LGV infection (solid squares) and 19 patients with an anal non-L biovar chlamydia infection (open squares). Except if indicated the patient groups differed significantly (*P* < 0.01). MOMP indicates major outer membrane protein; LPS, lipopolysaccharide; n.s., not significant. *Absence of patient reported discharge, pain, itch, incomplete defecation, or constipation.* <10 leucos/hpf = less than 10 leucocytes per high power field in a Gram-stained anal smear.

**TABLE 2.** Test Characteristics of the IgA Anti-MOMP Assay to Differentiate Anal LGV Infections From Non-LGV Chlamydia Anal Infections, in Asymptomatic Men Who Have Sex With Men, Amsterdam STI Outpatient Clinic

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Cut-off Titer</th>
<th>Ct+/LGV+</th>
<th>Ct+/LGV−</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Diagnostic Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No complaints</td>
<td>Negative/equivocal</td>
<td>6</td>
<td>14</td>
<td>73.9 (53.5–87.5)</td>
<td>93.3 (70.2–99.7)</td>
<td>39.7 (4.3–369.7)</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>17</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10 leucos/hpf</td>
<td>Negative/equivocal</td>
<td>2</td>
<td>6</td>
<td>85.7 (60.1–96.0)</td>
<td>75.0 (40.9–92.9)</td>
<td>18.0 (2.0–161.1)</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>12</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The assay was performed on 38 men with no complaints (the absence of patient reported discharge, pain, itch, incomplete defecation or constipation) and 22 with <10 leucos/hpf (less than 10 leucocytes per high power field in a Gram stained anal smear). Ct+/LGV+ indicates anal LGV biovar specific chlamydia infection; Ct+/LGV−, anal non-LGV biovar chlamydia infection; MOMP, major outer membrane protein; 95% CI, 95% confidence intervals.
on LGV, in which case biovar-specific C. trachomatis NAATs can be considered too expensive or too laborious to obtain.

For a correct NAAT-based LGV diagnosis, it is important to obtain a specimen from suspected mucosal lesions under anoscopic vision. If these requirements cannot be met, a serological assay could be used to make a presumptive LGV diagnosis. Moreover, a serology assay could be of additional value in the later stages of LGV when the pathogen possibly has become undetectable in the mucosal lining whereas the infection invaded into underlying connective tissue layers and lymphatics.

Other Serologic Assays to Diagnose LGV

Before biovar-specific NAAT became available, chlamydia cultivation was considered the gold standard for the confirmation LGV cases. Chlamydia cultivation is elaborate and lacks sensitivity. Therefore, serological assays like the Complement Fixation assay (a Chlamydia genus specific but not trachomatis-specific assay) and the microimmunofluorescence test (MIF, an IgG class chlamydia species-specific serologic assay) were then used as an alternative method for LGV diagnostic purposes. Nonetheless, false-positive results with serological confirmed LGV cases because of non-L biovar chlamydia anal infections in MSM were already reported by Schachter.

In the beginning of the recent LGV epidemic among MSM, we showed that the IgG anti-MOMP assay had a high positive predictive value for anal LGV infections in symptomatic patients but failed in asymptomatic cases. The use of a Whole immunofluorescence test based on crude LGV infected cells as antigen was proposed by Forrester et al, but this test is not standardized and not suitable for high throughput use. Anti-LPS assays performed worse compared with the anti-MOMP assays in our study. LPS-based chlamydia serology assays cross-react with other chlamydia species like the widely prevalent C. pneumonia species. As a consequence, LPS-based assays suffer from less specific results when used for C. trachomatis diagnostics.

The IgA class anti-MOMP test performed better compared with the IgG-based test to differentiate LGV from non-LGV infections (Table 1), even in asymptomatic patients. IgA class serological assays are considered to reflect active infections, whereas IgG class assays are a marker for both current and past infections. In a high-risk population for STI with
possible past infections this can lead to false-positive results and loss of specificity, as reflected in Table 1. Recently an IgA Chlamydia specific assay has been evaluated to diagnose anal LGV infections in a predominantly symptomatic population by van der Snoek et al.23 A sum score of the IgA antibody response and the patients’ age was used as diagnostic criterion and older age correlated with anal LGV infections. Epidemiologic characteristics like age depend on the diseased population and can change over time. Therefore, combining a serological outcome with age has its limitations for diagnostic and screening purposes in other populations. Moreover, the diagnostic value of this assay in an asymptomatic population is unknown.24

Asymptomatic LGV Proctitis Cases

A considerable proportion of LGV cases in this study were asymptomatic at the time of diagnosis. This is in contrast

![Figure 3. Sensitivity and specificity plot with the IgA anti-MOMP serologic assay to differentiate anal LGV infections from non-LGV chlamydia anal infections in 203 men who have sex with men, Amsterdam STI outpatient clinic. The assay was performed on 98 patients with an anal LGV infection and 105 patients with an anal non-LGV biovar chlamydia infection. Sensitivity (solid squares), specificity (open circles), and 95% confidence intervals (shaded area) are shown. The dotted lines indicate the cut-off points (1.1, 2.0, and 3.0) described in Table 3. MOMP indicates major outer membrane protein.]

### Table 3. Test Characteristics of the IgA Anti-MOMP Assay to Differentiate Anal LGV Infections From Non-LGV Chlamydia Anal Infections, in 203 Men Who Have Sex With Men, Amsterdam STI Outpatient Clinic

<table>
<thead>
<tr>
<th>Cut-off Titer</th>
<th>Ct+ / LGV+</th>
<th>Ct+ / LGV−</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>Diagnostic Odds Ratio (95% CI)</th>
</tr>
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<tr>
<td>≤1.1</td>
<td>21</td>
<td>77</td>
<td>78.6 (69.1–86.2)</td>
<td>61.0 (51.0–70.3)</td>
<td>65.3 (55.9–73.8)</td>
<td>75.3 (64.7–84.0)</td>
<td>5.7 (3.1–10.7)</td>
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<td>&gt;1.1</td>
<td>64</td>
<td>41</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤2.0</td>
<td>24</td>
<td>74</td>
<td>75.5 (65.8–83.6)</td>
<td>74.3 (64.8–82.3)</td>
<td>73.3 (63.5–81.6)</td>
<td>76.5 (67.0–84.3)</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>≤3.0</td>
<td>34</td>
<td>64</td>
<td>65.3 (55.0–74.6)</td>
<td>81.0 (72.1–88.0)</td>
<td>76.2 (65.7–84.8)</td>
<td>71.4 (62.4–79.3)</td>
<td>8.0 (4.2–15.2)</td>
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<tr>
<td>&gt;3.0</td>
<td>85</td>
<td>20</td>
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</tbody>
</table>

The assay was performed on 98 patients with an anal LGV infection (Ct+ / LGV+) and 105 patients with an anal non-LGV biovar chlamydia infection (Ct+ / LGV−).

MOMP indicates major outer membrane protein; Ct+ / LGV+, anal LGV biovar specific chlamydia infection; Ct+ / LGV−, anal non-LGV biovar chlamydia infection; 95% CI, 95% confidence intervals; <10 leucos/hpf, less than 10 leucocytes per high power field in a Gram stained anal smear.
to recent reports from Great Britain where only 5% (3/61) asymptomatic cases were found in a retrospective survey.25 Because of the retrospective data collection, recall bias could have caused over reporting of complaints experienced at the time of the clinic visit. This is supported by a prospective study performed at a large London clinic, where in 17% (6/35) asymptomatic LGV cases were found.26 In the London study, anal swabs were collected without anoscopy in asymptomatic cases. This could have affected the sensitivity of the diagnostic tests and missed additional asymptomatic LGV cases. In most studies on asymptomatic anal LGV infections, patient-reported symptoms are used to define symptomatic cases.25,26 This criterion is subjective but beneficial in situations lacking anoscopy. The presence of mucosal membrane abnormalities is an objective definition of symptomatic infections, but requires anoscopy.5,6,20 We chose not to use this definition in this study because previous investigations proved it lacks discriminative power from other anal infections commonly found in MSM, like gonorrhea and non-LGV chlamydia infections.6,19 A third definition for symptomatic anal infections is based on the presence of leucos/hp in anal smears. This criterion performs reasonably well as a predictor for anal LGV infections as we showed earlier.5 Therefore we added this definition to our analysis, although a drawback for diagnostic purposes is the required anoscopy and laboratory routine.

One of the strong points of this study is the long follow-up period of patients with anal chlamydia infections; such data has not been reported previously. Although the IgA anti-MOMP reactivity dropped significantly 52 weeks after treatment, the COI titer remained well above the titer associated with LGV infections (Fig. 2). Thus, the assay seems not suitable to differentiate past effectively treated infections from successive reinfections, at least in the past year. We conclude that the IgA anti-MOMP assay can detect a considerable portion of the anal LGV infections in both symptomatic and asymptomatic MSM STI clinic visitors. Yet the serologic assay is not suitable for clinical diagnostic purposes and biovar L specific NAAT remain a superior and preferable diagnostic test for LGV infections. As screening tool in population based surveys, the IgA anti-MOMP assay in combination with a routine (biovar nonspecific) chlamydia NAAT test could be used to make a presumptive diagnosis of LGV.

REFERENCES


