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## The sensitivities and specificities of total plasma protein and plasma fibrinogen for the diagnosis of traumatic reticuloperitonitis in cattle

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### Abstract

We performed a prospective clinical study to select cut-off points for total plasma protein (TPP) and plasma fibrinogen (PF) to differentiate between traumatic reticuloperitonitis (TRP) and other gastrointestinal diseases with similar clinical signs, and to estimate the dependence and accuracy of TPP and PF when used in series or in parallel. TPP and PF were estimated preoperatively by refractometry in 93 cattle with TRP and 65 cattle with gastrointestinal diseases such as vagus indigestion ( $n = 16$ ), liver abscesses ( $n = 17$ ), omasal impaction ( $n = 19$ ) and Johne's disease ( $n = 13$ ). Three different cut-off points were selected by two-graph receiver-operating characteristic (TG-ROC) analysis for TPP and PF. Conditional covariances were calculated as a measure of dependence between sensitivities and specificities of TPP and PF. The cut-off points of 7.22, 7.78 and 8.82 g/dl for TPP and 622, 691 and 766 mg/dl for PF were suggested by TG-ROC based on different requirements of test performances. There was moderate negative dependence between sensitivities of TPP and PF at the 8.82 g/dl and 766 mg/dl cut-off points, and mild negative dependence between their specificities at the 7.78 g/dl and 691 mg/dl cut-off points, respectively. Acceptable accuracy (98 or 86% specificity with 62 or 88% sensitivity, respectively) was obtained with serial interpretation of the tests.

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**Keywords:** Traumatic reticuloperitonitis; Total plasma protein; Plasma fibrinogen; Sensitivity; Specificity; Cattle

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## 1. Introduction

Traumatic reticuloperitonitis (TRP) is a sporadic disease of ruminants that is caused by perforation of the reticulum by ingested foreign materials; it is a common reason for abdominal surgery in cattle. The complexity of development and the possibility that a number of syndromes can occur together makes the tentative diagnosis difficult. In practice, the diagnosis is mainly made by physical examination—although additional diagnostic methods (such as hematologic tests, abdominocentesis, radiography, ultrasonography, laparoscopy or exploratory laparoruminotomy) might be used. Because complications of the disease are frequent, a more-accurate indication of its presence or severity would be valuable. There is an increase in total plasma protein (TPP) and plasma fibrinogen (PF) levels among cattle with TRP and those with other gastrointestinal diseases (Samadieh et al., 1978; Dubensky and White, 1983; Nowrouzian et al., 1991; Smith, 1993; Ward and Ducharme, 1994; Hirvonen and Pyörälä, 1998; Smith and Slenning, 2000).

Our purpose of this study was to select TPP and PF cut-off points for differentiating TRP from other gastrointestinal diseases (vagus indigestion, liver abscesses, omasal impaction and Johne's disease) that might be confused with TRP. In addition, we estimated the dependence and accuracy of TPP and PF when they are used in combination for TRP diagnosis.

## 2. Materials and methods

### 2.1. Procedure

We performed a prospective clinical study on all Holstein dairy cattle with gastrointestinal diseases referred to the Veterinary Teaching and Research Hospital of Faculty of Veterinary Medicine, University of Tehran during a 1-year period (from October 2001 to September 2002) from dairies around Tehran city. Blood samples of 158 cattle with gastrointestinal diseases (TRP, vagus indigestion, liver abscesses, omasal impaction and Johne's disease) were taken preoperatively. TPP and PF concentrations were obtained by refractometry, which is a simple and accurate method (Calloway et al., 2002; George, 2001; George and O'Neill, 2001). The disorders were confirmed at exploratory laparotomy or surgical intervention.

### 2.2. Statistical analysis

To select TPP and PF cut-off points, the data were submitted to the two-graph receiver-operating characteristic (TG-ROC) analysis (Greiner, 1995) which is a plot of the test sensitivity (Se) and specificity (Sp) against the cut-off value (assuming the later to be an independent variable). Valid pairs of Se and Sp can be read for pre-assigned (e.g. "target") cut-off values directly from the TG-ROC plots. Approximately equal test parameters (Se and Sp) can be obtained from the intersection point of two graphs. When the value for approximately equal Se and Sp is below the preselected (target) accuracy (95%), two alternative cut-offs also are suggested by TG-ROC to represent the Se or Sp above target

(Greiner et al., 1995). Because TPP and PF measures are similar biologic processes, we expected that test results were dependent, conditional on the animal's disease status; we calculated the conditional covariances (Gardner et al., 2000). Statistical significance of the calculated covariances was evaluated by chi-square test. The performance of TPP and PF in serial- and parallel-interpretation schemes at these same three pairs of cut-off points was calculated. Kappa also was calculated (Gardner et al., 2000).

### 3. Results

TRP was confirmed in 93 of cattle at exploratory laparotomy or surgical intervention, and 65 cattle found to have vagus indigestion (16 cases), liver abscesses (17 cases), omasal impaction (19 cases) and Johne's disease (13 cases) (Table 1).

The curves of Se and Sp of the TPP and PF as a function of the applied cut-off points are shown in Figs. 1 and 2, respectively. The intersection points of the two curves in Figs. 1 and 2 indicate that with cut-off points of 7.78 g/dl for TPP and 691 mg/dl for PF, respectively, similar Se and Sp for TPP and PF would be achieved. Based on our targets for test performance, Table 2 shows the evaluation indices for TPP and PF under different cut-off points selected by TG-ROC.

Conditional covariances as a measure of dependence between TPP and PF at the three different cut-off points were calculated. Because the covariances do not provide a direct measure of the magnitude of dependence, they are also expressed as a proportion of their maximum possible values. Kappa also was calculated for the TRP and other-diseases groups (Table 3). There was significant moderate negative dependence between sensitivities of TPP and PF at 8.82 g/dl and 766 mg/dl cut-off points, and significant mild negative dependence between their specificities at the 7.78 g/dl and 691 mg/dl cut-off points, respectively.

Based on the different targets for test performance, the Se and Sp of TPP and PF in serial- and parallel-interpretation schemes at different cut-off points are shown in Table 4. By serial interpretation of TPP and PF, the Sp of 98 or 86% was obtained with the Se of 62 or 88%, respectively.

Table 1

Descriptions of total plasma protein (TPP) and plasma fibrinogen (PF) in Holstein dairy cattle with traumatic reticuloperitonitis (TRP) or other gastrointestinal diseases (vagus indigestion, liver abscesses, omasal impaction and Johne's disease)

Measure	TRP ( <i>n</i> = 93)	Other diseases ( <i>n</i> = 65)
TPP (g/dl)		
Minimum	6.14	4.01
Mean (S.D.)	8.40 (0.07)	6.64 (0.16)
Median	8.50	6.73
Maximum	9.87	9.30
PF (mg/dl)		
Minimum	568	339
Mean (S.D.)	770 (9.34)	606 (12.1)
Median	780	613
Maximum	930	789

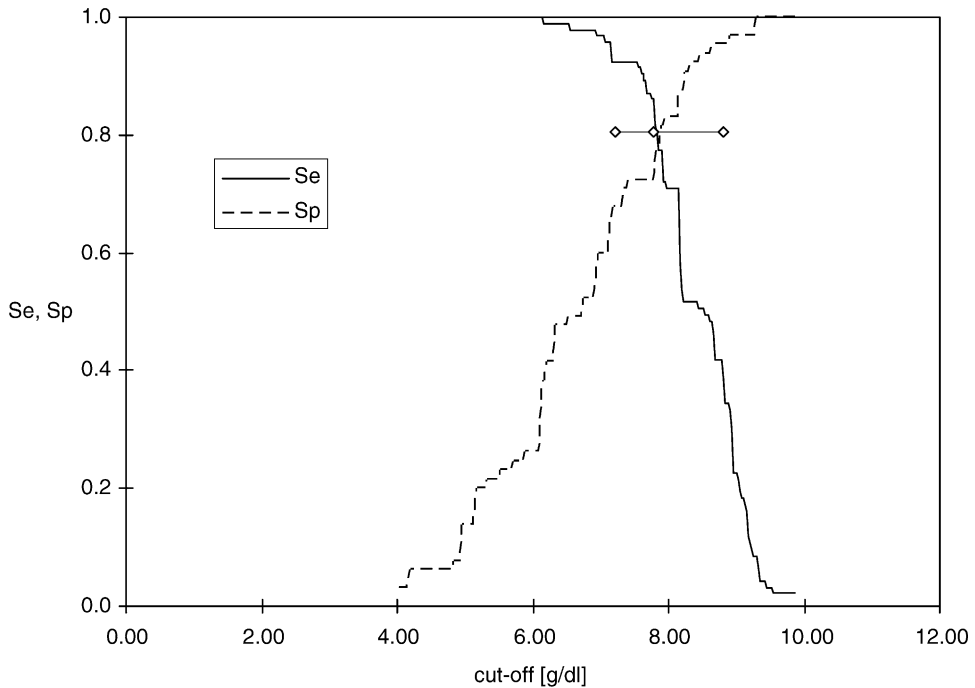


Fig. 1. TG-ROC analysis of TPP. The intersection point of the two-graph ROC curve indicates the cut-off point (7.78 g/dl) at which approximately equivalent Se and Sp can be achieved. Because the value for approximately equal Se and Sp is below the preselected (target) accuracy (95%), cut-off point values of 7.22 and 8.82 g/dl are suggested by TG-ROC to represent the Se and Sp above the preselected level, respectively.

#### 4. Discussion

The clinical signs of TRP are similar to those for many diseases associated with gastrointestinal tract such as vagus indigestion, liver abscesses, omasal impaction and Johne's disease in cattle (Belknap and Navarre, 2000). Dependence of TPP and PF at different cut-off points in differentiating between TRP and other gastrointestinal diseases has not been studied before.

The TPP and PF concentrations required to differentiate TRP from other gastrointestinal diseases with high Sp had such low sensitivities (34 and 55%, respectively), that measuring either TPP or PF alone was of limited usefulness for differentiating between TRP and other gastrointestinal diseases (Dubensky and White, 1983; Nowrouzian et al., 1991; Smith, 1993; Hirvonen and Pyörälä, 1998; Moghaddam et al., 1999; Smith and Slenning, 2000).

When more than one test is available, the serial interpretation scheme (positive on both tests is positive, negative otherwise) might maximize the Sp of diagnosis. However, dependence between the sensitivities and specificities of pairs of tests affects the Se and Sp of tests when used in combination. Compared with values expected if tests are conditionally independent, a positive dependence in test Se reduces the Se of parallel-test

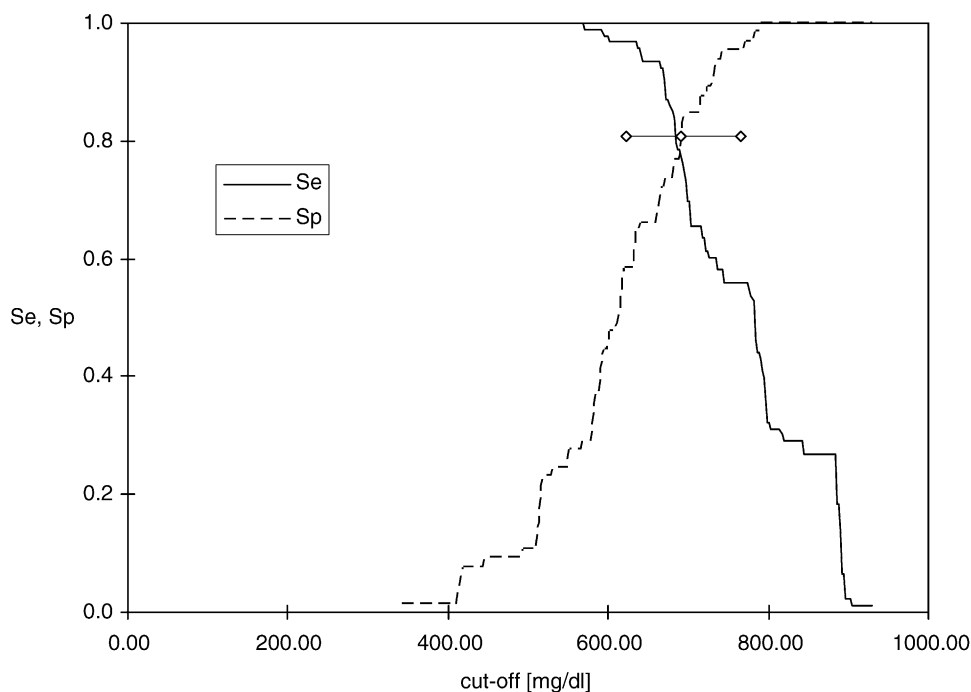


Fig. 2. TG-ROC analysis of PF. The intersection point of the two-graph ROC curve indicates the cut-off point (691.05 mg/dl) at which approximately equivalent Se and Sp can be achieved. Because the value for approximately equal Se and Sp is below the preselected (target) accuracy (95%), cut-off point values of 622 and 766 mg/dl are suggested by TG-ROC to represent the Se and Sp above the preselected level, respectively.

interpretation (positive on at least one test is positive, negative otherwise) and a positive dependence in test Sp reduces the Sp of serial interpretation (Gardner et al., 2000).

Calculation of conditional covariances for TPP and PF revealed dependence between their sensitivities and specificities at some cut-off points. There was moderate negative

Table 2

Performance of TPP and PF (for diagnosing traumatic reticuloperitonitis in cattle) at different cut-off points, when used singly

Cut-off point	Sensitivity (%)	Specificity (%)
TPP (g/dl)		
8.82	34	95
7.78	81	72
7.22	92	67
PF (mg/dl)		
766	55	95
691	77	76
622	96	60

Table 3

Test covariances, covariances expressed as a proportion of their maximum values and kappa at different cut-off points of TPP and PF (for traumatic reticuloperitonitis in cattle)

Cut-off point		Sensitivity			Specificity		
TPP (g/dl)	PF (mg/dl)	Covariance	Covariance/maximum possible covariance	Kappa	Covariances	Covariance/maximum possible covariance	Kappa
8.82	766	-0.057 <sup>a</sup>	0.37	-0.22	-0.0025	0.05	-0.05
7.78	691	0.0063	0.04	0.04	-0.047 <sup>a</sup>	0.27	-0.24
7.22	622	0.0068	0.18	0.11	-0.039	0.19	-0.16

<sup>a</sup> Covariance was significantly ( $P < 0.05$ ) different from 0.

Table 4

Performance of TPP and PF in serial- and parallel-interpretation schemes based on the different cut-off points (accuracy for diagnosing traumatic reticuloperitonitis in cattle)

Cut-off point		Serial-interpretation scheme		Parallel-interpretation scheme	
TPP (g/dl)	PF (mg/dl)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
8.82	766	13	99	76	90
7.78	691	62	98	95	50
7.22	622	88	86	99	40

dependence between sensitivities of 8.82 g/dl TPP and 766 mg/dl PF. This results in even-higher Se of parallel testing compared to assuming conditional independence. There was significant mild negative dependence between specificities of 7.78 g/dl TPP and 691 mg/dl PF, which results in even-higher Sp of serial testing compared to assuming conditional independence. A high Sp (98%) of serial testing of TPP and PF at 7.78 g/dl and 691 mg/dl cut-off points, respectively, can be achieved with Se of 0.62. However, with cut-off points of 7.22 g/dl and 622 mg/dl for TPP and PF, the acceptable Se and Sp of 88 and 86%, respectively, can be gained by serial testing.

## 5. Conclusion

The results of this study demonstrated that serial interpretation of TPP and PF with suggested cut-off points is useful for differentiating TRP from vagus indigestion, liver abscesses, omasal impaction and Johne's disease in cattle.

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