

IFITM1, CD10, SMA, and h-caldesmon as a helpful combination in differential diagnosis between endometrial stromal sarcoma and cellular leiomyoma

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Research

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Abstract

The differential diagnosis of endometrial stromal sarcoma (ESS) and uterine cellular leiomyoma (CL) remains a challenge in clinical practice. Cluster of differentiation 10 (CD10) and smooth muscle actin (SMA) are commonly used in the differential diagnosis of ESS and CL. However, the current combination of immunohistochemical antibodies has been shown to be inaccurate, suggesting the need for novel immunomarkers panels for differentiating between ESS and CL. Interferon-induced transmembrane protein 1 (IFITM1) is a novel immunomarker for endometrial stromal cells, h-caldesmon is an immunomarker for smooth muscle cells and has a higher specificity than SMA. So this study aimed to investigate IFITM1, CD10, SMA, and h-caldesmon as a useful combination of biomarkers for diagnosing between ESS and CL. Tissue microarrays were used to detect IFITM1, CD10, SMA, and h-caldesmon immunohistochemical staining in 30 ESS and 33 CL cases. The expressions of IFITM1 and CD10 were high in ESS (86.7% and 63.3%, respectively) but low in CL (18.2% and 21.2%), whereas those of h-caldesmon and SMA were high in both CL (87.9% and 100%) and low in ESS (6.9% and 40%). In diagnosing ESS, IFITM1 had better sensitivity and specificity (86.7% and 81.8%, respectively) than CD10 (63.3% and 78.8%). The specificity of h-caldesmon in diagnosing CL was significantly higher (93.1%) than that of SMA (60%). When all four antibodies were combined for the differential diagnosis, the area-under-the-curve predictive value was 0.995. The most sensitive and specific combinations for diagnosing ESS were IFITM1(+) or CD10(+) and h-caldesmon(-) (sensitivity 86.7%, specificity 93.9%), IFITM1(+) and h-caldesmon(-) ((sensitivity 80%, specificity 100%). The most sensitive and specific combinations for diagnosing CL were h-caldesmon(+) and SMA(+)(sensitivity 87.9%, specificity 100%), h-caldesmon(+) or SMA(+) and IFITM1(-)(sensitivity 81.8% , specificity 93.1%).Therefore, IFITM1, CD10, SMA, and h-caldesmon are a good combination of biomarkers for the differential diagnosis of ESS and CL.

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caldesmon(-) ((sensitivity 80%, specificity 100%). The most sensitive and specific combinations for diagnosing CL were h-caldesmon(+) and SMA(+)(sensitivity 87.9%, specificity 100%), h-caldesmon(+) or SMA(+) and IFITM1(-)(sensitivity 81.8% , specificity 93.1%).Therefore, IFITM1, CD10, SMA, and h-caldesmon are a good combination of biomarkers for the differential diagnosis of ESS and CL.The differential diagnosis of endometrial stromal sarcoma (ESS) and uterine cellular leiomyoma (CL) remains a challenge in clinical practice. Cluster of differentiation 10 (CD10) and smooth muscle actin (SMA) are commonly used in the differential diagnosis of ESS and CL. However, the current combination of immunohistochemical antibodies has been shown to be inaccurate, suggesting the need for novel immunomarkers panels for differentiating between ESS and CL. Interferon-induced transmembrane protein 1 (IFITM1) is a novel immunomarker for endometrial stromal cells, h-caldesmon is an immunomarker for smooth muscle cells and has a higher specificity than SMA. So this study aimed to investigate IFITM1, CD10, SMA, and h-caldesmon as a useful combination of biomarkers for diagnosing between ESS and CL. Tissue microarrays were used to detect IFITM1, CD10, SMA, and h-caldesmon immunohistochemical staining in 30 ESS and 33 CL cases. The expressions of IFITM1 and CD10 were high in ESS (86.7% and 63.3%, respectively) but low in CL (18.2% and 21.2%), whereas those of h-caldesmon and SMA were high in both CL (87.9% and 100%) and low in ESS (6.9% and 40%). In diagnosing ESS, IFITM1 had better sensitivity and specificity (86.7% and 81.8%, respectively) than CD10 (63.3% and 78.8%). The specificity of h-caldesmon in diagnosing CL was significantly higher (93.1%) than that of SMA (60%). When all four antibodies were combined for the differential diagnosis, the area-under-the-curve predictive value was 0.995. The most sensitive and specific combinations for diagnosing ESS were IFITM1(+) or CD10(+) and h-caldesmon(-) (sensitivity 86.7%, specificity 93.9%), IFITM1(+) and h-caldesmon(-) ((sensitivity 80%, specificity 100%). The most sensitive and specific combinations for diagnosing CL were h-caldesmon(+) and SMA(+)(sensitivity 87.9%, specificity 100%), h-caldesmon(+) or SMA(+) and IFITM1(-)(sensitivity 81.8% , specificity 93.1%).Therefore, IFITM1, CD10, SMA, and h-caldesmon are a good combination of biomarkers for the differential diagnosis of ESS and CL.

Background

Endometrial stromal sarcoma (ESS) is a rare malignant mesenchymal tumor of the uterine. In 2014, the World Health Organization classified ESS as low-grade ESS, high-grade ESS, and undifferentiated endometrial sarcoma[1]. However, there is a overlap in morphology and immunohistochemistry between ESS and leiomyoma, especially for the low grade ESS from cellular leiomyoma (CL). Currently, cluster of differentiation 10 (CD10) has been considered as the best immunomarker for endometrial stromal cells[2–6], but it not expressed in all mesenchymal tumors[7–9]. Rather, CD10 is sometimes expressed in leiomyoma[10, 11]. Smooth muscle actin (SMA) is a common biomarker for smooth muscle, however, SMA is sometimes expressed in ESS [12–15], suggesting the need for novel immunomarkers and immunohistochemical panels for differentiating between ESS and CL.

Interferon-induced transmembrane protein 1 (IFITM1), also called CD225, is a novel immunomarker for endometrial stromal cells and tumors[16, 17] and outperforms CD10 in distinguishing LG ESS from CL[18, 19]. Meanwhile, h-caldesmon is an immunomarker for smooth muscle cells and has a higher specificity

than smooth muscle actin (SMA). However, there has been no study on the combined use of IFITM1, CD10, SMA, and h-caldesmon in distinguishing between ESS and CL. This study aimed to investigate IFITM1, CD10, SMA, and h-caldesmon as a useful combination of biomarkers for the differential diagnosis of ESS and CL.

Materials And Methods

The study were approved by the Review Boards of First Affiliated Hospital, Shihezi University School of Medicine and Xinjiang Uygur Autonomous Region People's Hospital.

Clinical data

This study enrolled 30 patients with ESS (5 with endometrial stromal nodules, 16 with LG ESS, 5 with high-grade ESS, and 4 with undifferentiated endometrial sarcoma) and 33 patients with CL. Data were collected from 2012 to 2017 from the Department of Pathology of the First Affiliated Hospital of Shihezi University School of Medicine and the Department of Pathology of Xinjiang Uygur Autonomous Region People's Hospital. The average age of 30 ESS patients was 49.8 (27–73) years, and the main clinical symptoms were irregular vaginal bleeding, abdominal pain, postmenopausal vaginal bleeding, and uterine fibroids. The 33 CL patients had an average age of 40.2 (26–60) years and mainly showed clinical manifestations of dysmenorrhea, prolonged menstrual period, and increased menstrual volume. All pertinent clinical information was obtained from the hospital electronic medical records. All patients had complete medical history and clinicopathologic data, and all cases were confirmed by surgery and pathology.

Tissue microarray building

Paraffin blocks and corresponding hematoxylin and eosin (HE)-stained sections were collected, and the HE-stained sections were evaluated by two senior pathologists. Morphologically representative regions were carefully selected on each individual paraffin-embedded block, and a hollow needle (1.0 mm diameter) was used to puncture the selected area to a new small wax block. Considering the specificity of the tumor and the tendency of the paraffin tissue to flake off, two punctures were performed in different areas of each tumor wax block.

Immunohistochemistry

For immunohistochemical analysis, biopsy specimens were fixed in 10% neutral-buffered formalin and routinely processed. The paraffin-embedded blocks were sectioned (4 μ m thickness), stained with HE, and observed by microscopy. The two-step immunohistochemical EnVision method was applied. The primary antibodies used are listed in Table 1. The extent of staining was evaluated as 0%, 0–25%, 26–50%, 51–75%, and 76–100%, and the intensity of staining as absent (0), weak (1+), moderate (2+), and strong (3+). The second staining was conducted after 1 month, and the results were interpreted as described above. When a different staining evaluation was used, the higher intensity score was used as the final score.

Table 1

Commercial Sources and Characteristics of IFITM1,CD10,h-caldesmon and SMA Antibodies.

Name	Dilution	Company	Antigen retrieval	Location
IFITM1	1:400	Sigma	citrate	Nucleus/plasma
CD10	1:50	ZSGB-BIO	EDTA	Cytoplasm/membrane
SMA	1:100	ZSGB-BIO	citrate	Cytoplasm
h-caldesmon	1:100	ZSGB-BIO	citrate	Cytoplasm

Statistical analysis

Differences between the two groups were compared using the chi-squared test. The sensitivity, specificity, and positive predictive values (PPVs) were calculated from the screening and diagnostic tests. The staining score was obtained by multiplying the extent with the intensity, and the resulting score was used for the receiver operating characteristic curve. All statistical analyses were performed using SPSS version 17.0. A p-value of < 0.05 was considered as statistically significant.

Results

The immunohistochemical results are summarized in Table 2 and illustrated in Fig. 1. The sensitivity, specificity, PPVs, and negative predictive values (NPVs) are summarized in Tables 3–6 and shown in Figs. 2–4.

Table 2

Intensity and Extent of Immunohistochemical Staining of IFITM1,CD10,h-caldesmon and SMA in endometrial stromal sarcoma and cellular leiomyoma.

Antibodies	ESS(30 cases)				CL(33 cases)					
	Positive	Category Intensity				Positive	Category Intensity			
		0	1+	2+	3+		0	1+	2+	3+
IFITM1	26(86.7%)	4	10	8	8	6(18.2%)	27	6	0	0
CD10	19(63.3%)	11	6	7	6	7(21.2%)	26	7	0	0
h-caldesmon	2(6.7%)	28	2	0	0	29(87.9%)	4	15	10	4
SMA	12(40%)	18	4	6	2	33(100%)	0	22	9	2

Abbreviations: ESS indicates Endometrial Stromal Sarcomas; CL indicates Cellular Leiomyoma.

Table 3

Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of IFITM1 and CD10 for endometrial stromal sarcoma.

Antibodies	Sensitivity (%)	Specificity (%)	PPV(%)	NPV(%)
IFITM1	86.7	81.8	81.3	87.1
CD10	63.3	78.8	73.1	70.3
Abbreviations: PPV indicates Positive Predictive Value, NPV indicates Negative Predictive Value.				

IFITM1 and CD10

Both ESS (Fig. 1-A) and CL cases (Fig. 1-B) showed a dense spindle-cell braid-like arrangement. Among the 30 ESS cases, 26 (86.7%) demonstrated IFITM1 nuclear positivity (Fig. 1-C). The staining intensity was strong (3+) in 8 cases, moderate (2+) in 8 cases, and weak (1+) in 10 cases. The average intensity score was 1.7. Of the 33 CL cases, only 6 (18.2%) demonstrated IFITM1 nuclear positivity (Fig. 1-D), all of which scored weak (1+) in intensity. CD10 was expressed in 19 (63.3%) of the 30 ESS cases (Fig. 1-E). The staining in these cases occurred in the cell cytoplasm and was strong (3+) in 6 cases, moderate (2+) in 7 cases, and weak (1+) in 6 cases. The average intensity score was 1.3. Only 7 (21.2%) of the 33 CL cases were CD10(+), and all positive cases had a weak (1+) intensity (Fig. 1-F).

SMA and h-caldesmon

SMA was positive in 12 (40%) of the 30 ESS cases (Fig. 1-G). The staining in these cases was expressed in the cytoplasm and was moderate to strong (2+ to 3+) in 8 cases and weak (1+) in 4 cases. All 33 (100%) CL cases expressed SMA (Fig. 1-H), and among them, the staining was moderate to strong (2+ to 3+) in 11 cases and weak (1+) in the remaining cases. The average intensity score was 1.7. Meanwhile, h-caldesmon was expressed in the cell cytoplasm of only 2 (6.7%) of the 30 ESS cases (Fig. 1-I), and the staining in these positive cases were weak (1+). However, 29 (87.9%) of the 33 CL cases exhibited h-caldesmon positivity (Fig. 1-J). In these 33 CL cases, the staining was strong (3+) in 4 cases, moderate (2+) in 10 cases, and weak (1+) in 15 cases. The average intensity score was 1.4.

Sensitivity, specificity, PPVs, and NPVs of IFITM1, CD10, h-caldesmon, and SMA

In the diagnosis of ESS, IFITM1 showed a sensitivity of 86.7%, a specificity of 81.8%, a PPV of 81.3%, and an NPV of 87.1%. For CD10, the sensitivity, specificity, PPV, and NPV were 63.3%, 78.8%, 73.1%, and 70.3%, respectively. h-caldesmon positivity may support a diagnosis of CL, showing a sensitivity of 87.9%, a specificity of 93.3%, a PPV of 93.5%, and an NPV of 87.5%. SMA had the highest sensitivity (100%), but its specificity was 60%, significantly lower than that of h-caldesmon. SMA had a PPV and an NPV of 73.3% and 100%, respectively (Tables 3 and 4).

Table 4

Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of h-caldesmon and SMA for cellular leiomyoma.

Antibodies	Sensitivity (%)	Specificity (%)	PPV(%)	NPV(%)
h-caldesmon	87.9	93.3	93.5	87.5
SMA	100.0	60.0	73.3	100.0

Abbreviations: PPV indicates Positive Predictive Value, NPV indicates Negative Predictive Value.

IFITM1, CD10, h-caldesmon, and SMA as a useful combination for differential diagnosis

Based on the expressions of the four antibodies and their receiver operating characteristic curve (the area-under-the-curve predictive value was 0.995 (Fig. 2), we speculate that their combinations could be helpful in the differential diagnosis of ESS and CL.

When all four antibodies were combined for the ESS diagnosis (Table 5, Fig. 3), The most sensitive combination was IFITM1(+) or CD10(+), IFITM1(+) or CD10(+) and h-caldesmon(-), IFITM1(+) and h-caldesmon(-), with a sensitivity of 93.3%, 86.7%, 80%, respectively (Fig. 3-A). The combination of antibodies greatly increased the specificity of ESS diagnosis (Fig. 3-B), the specificity of combinations of IFITM1(+) and h-caldesmon(-), IFITM1(+) and SMA(-), IFITM1(+) and CD10(+) and h-caldesmon(-), IFITM1(+) and CD10(+) and h-caldesmon(-) and SMA(-), and IFITM1(+) or CD10(+) and h-caldesmon(-) and SMA(-) were 100%. Considering both sensitivity and specificity, the combination with the best diagnostic value for ESS was IFITM1(+) or CD10(+) and h-caldesmon(-), with a sensitivity and a specificity of 86.7% and 93.9%, respectively.

Table 5

The Sensitivity and Specificity of combined IFITM1, CD10, h-caldesmon and SMA immunostaining in the Diagnosis of endometrial stromal sarcoma.

Groups	Sensitivity (%)	Specificity (%)
IFITM1(+) and h-caldesmon(-) for ESS	80.0	100.0
IFITM1(+) and SMA(-) for ESS	60.0	97.0
CD10(+) and h-caldesmon(-) for ESS	50.0	100.0
CD10(+) and SMA(-) for ESS	36.7	100.0
IFITM1(+) and CD10(+) for ESS	56.7	93.9
IFITM1(+) or CD10(+) for ESS	93.3	66.7
IFITM1(+) or CD10(+) and h-caldesmon(-) for ESS	86.7	93.9
IFITM1(+) and CD10(+) and h-caldesmon(-) for ESS	53.3	100.0
IFITM1(+) or CD10(+) and SMA(-) for ESS	56.7	100.0
IFITM1(+) and CD10(+) and SMA(-) for ESS	30.0	100.0
IFITM1(+) and CD10(+) and h-caldesmon(-) and SMA(-) for ESS	31.0	100.0
IFITM1(+) or CD10(+) and h-caldesmon(-) and SMA(-) for ESS	56.7	100.0
Abbreviations: ESS indicates Endometrial Stromal Sarcomas.		

In diagnosing CL (Table 6, Fig. 4), the combinations h-caldesmon(+) or SMA(+), h-caldesmon(+) and SMA(+), and h-caldesmon(+) or SMA(+) and IFITM1(-) showed better sensitivity for differentiating CL from ESS, with sensitivity values of 100%, 87.9%, and 81.8%, respectively (Fig. 4-A). On the other hand, h-caldesmon(+) and IFITM1(-), h-caldesmon(+) and SMA(+), h-caldesmon(+) and SMA(+) and IFITM1(-), and h-caldesmon(+) and SMA(+) and IFITM1(-) and CD10(-) showed better specificity for predicting CL from ESS, with all specificity were 100% (Fig. 4-B). Taking into account both sensitivity and specificity, h-caldesmon(+) and SMA(+) was the best combination for distinguishing CL from ESS, with a sensitivity of 87.9% and a specificity of 100%. The second best combination for distinguishing CL from ESS was h-caldesmon(+) or SMA(+) and IFITM1(-), with a sensitivity of 81.8% and a specificity of 93.1%.

Table 6

The Sensitivity and Specificity of combined IFITM1,CD10,h-caldesmon and SMA immunostaining in the Diagnosis of cellular leiomyoma.

Groups	Sensitivity (%)	Specificity (%)
h-caldesmon(+) and IFITM1(-) for CL	69.7	100.0
SMA(+) and IFITM1(-) for CL	81.8	93.1
h-caldesmon(+) and CD10(-) for CL	72.7	96.6
SMA(+) and CD10(-) for CL	78.8	82.8
h-caldesmon(+) and SMA(+) for CL	87.9	100.0
h-caldesmon(+) or SMA(+) for CL	100.0	57.1
h-caldesmon(+) and SMA(+) and IFITM1(-) for CL	69.7	100.0
h-caldesmon(+) or SMA(+) and IFITM1(-) for CL	81.8	93.1
h-caldesmon(+) and SMA(+) and CD10(-) for CL	72.7	96.6
h-caldesmon(+) or SMA(+) and CD10(-) for CL	78.8	82.8
h-caldesmon(+) and SMA(+) and IFITM1(-) and CD10(-) for CL	57.6	100.0
h-caldesmon(+) or SMA(+) and IFITM1(-) and CD10(-) for CL	66.7	93.1
Abbreviations: CL indicates cellular leiomyoma.		

Discussion

The standard routine immunomarker panel used by most pathologists to distinguish ESS from CL consists of CD10, h-caldesmon, and SMA [10, 20–22], and an immunoprofile of CD10(+), h-caldesmon(-), and SMA(-) supports the diagnosis of ESS [15]. However, the current combination of immunohistochemical antibodies has been shown to be inaccurate, especially when diagnosing endometrial stromal tumors using CD10 alone [3, 10]. CD10 is not merely expressed in endometrial stromal tumors but is also positively expressed in 20–30% of smooth muscle tumors [13, 15]. SMA is a common muscle marker for endometrial stromal tumors and therefore has a very low specificity. Although h-caldesmon has a higher specificity than SMA, its sensitivity is worse [10, 13, 15, 23]. Thus, the need for a novel biomarker or a new immunohistochemical combination is imperative.

IFITM1 is a novel biomarker for endometrium stromal cells and is reported to be more valuable than CD10 [19, 24]. According to Busca et al [19], IFITM1 and CD10 were expressed in 14 ESS cases, and although their sensitivities were 83% and 91%, respectively, IFITM1 showed a higher specificity than CD10, that is, 70% vs. 45%. These findings are consistent with our findings, which state that IFITM1 was more specific and sensitive than CD10 in endometrial stromal tumors (sensitivity 86.7% vs. 63.3%, specificity 81.8% vs.

78.8%). Rush et al.[13] compared the expressions of SMA and h-caldesmon between ESS and CL and found that SMA was more sensitive than h-caldesmon (90.9% vs. 72.7%); however, h-caldesmon was more specific than SMA (100% vs. 91.7%). In our study, h-caldesmon showed a lower sensitivity than SMA (87.9% vs. 100%), but its specificity was significantly higher (93.3% vs. 60%).

Based on the expressions of the four antibodies and their receiver operating characteristic curve, we speculate that their combination could be useful in the clinical and differential diagnosis of ESS and CL. When such combination was used for diagnosis, the area-under-the-curve predictive value was 0.995. However, there are certain limitations in that the receiver operating characteristic curve cannot completely show the positive and negative expressions of the antibodies. We therefore compared the sensitivities and specificities of the four combined antibodies using a screening test and selected the best biomarker panel. For the diagnosis of ESS, the combination IFITM1(+) or CD10(+) had the highest sensitivity (93.3%), followed by IFITM1(+) or CD10(+) and h-caldesmon(-) (86.7%). In terms of specificity, the combinations IFITM1(+) and h-caldesmon(-), IFITM1(+) and SMA(-), and CD10(+) and SMA(-) were the best panels, having a specificity of up to 100%, while IFITM1(+) or CD10(+) was the worst panel, with a specificity of only 66.7%. Considering both sensitivity and specificity, the best panel for diagnosing ESS was IFITM1(+) or CD10(+) and h-caldesmon(-), with a sensitivity of 86.7% and a specificity of 93.9%. The other good predictive panel for distinguishing ESS from CL was IFITM1(+) and h-caldesmon(-), with a sensitivity of 80% and a specificity of 100%.

In general, no one immunomarker is sensitive and specific enough to make an accurate diagnosis, and so we usually use an immunohistochemical panel for differential diagnosis. This study revealed that the combination of IFITM1, CD10, SMA, and h-caldesmon comprised the best immunohistochemical panel for differentiating between ESS and CL. Considering the costs, we also recommend the combinations IFITM1 and h-caldesmon for the same purpose.

Conclusion

Immunohistochemical combinations of the novel antibody IFITM1 with traditional antibodies CD10, SMA, and h-caldesmon can be very useful in distinguishing ESS from CL, especially when the clinical history and histological morphology cannot be differentiated totally.

Declarations

Acknowledgments

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Ethics approval and consent to participate

Ethical approval was obtained from the Institutional Ethics Review Board (IERB) of the First Affiliated Hospital of School of Medicine, Shihezi University. Research was conducted according to all ethical standards, and written informed consent was obtained from all patients.

Consent for publication

Consent to publish has been obtained from all authors.

Availability of data and materials

All data in our study are available upon request.

Competing interests

The authors have no conflicts of interest to declare. No funding or other benefits related to the subject of this article were received from any commercial entity.

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Authors' contributions

ZH, SZZ and WC conceived and designed this study; CM provided the clinical specimens; ZWL, JXH and XX performed the experiments; SXH, JW and TL acquired the data; ZWL and CM analyzed the data and results; ZWL wrote the manuscript; ZH and PLJ improved and revised the manuscript. All authors read and approved the final manuscript.

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Figures

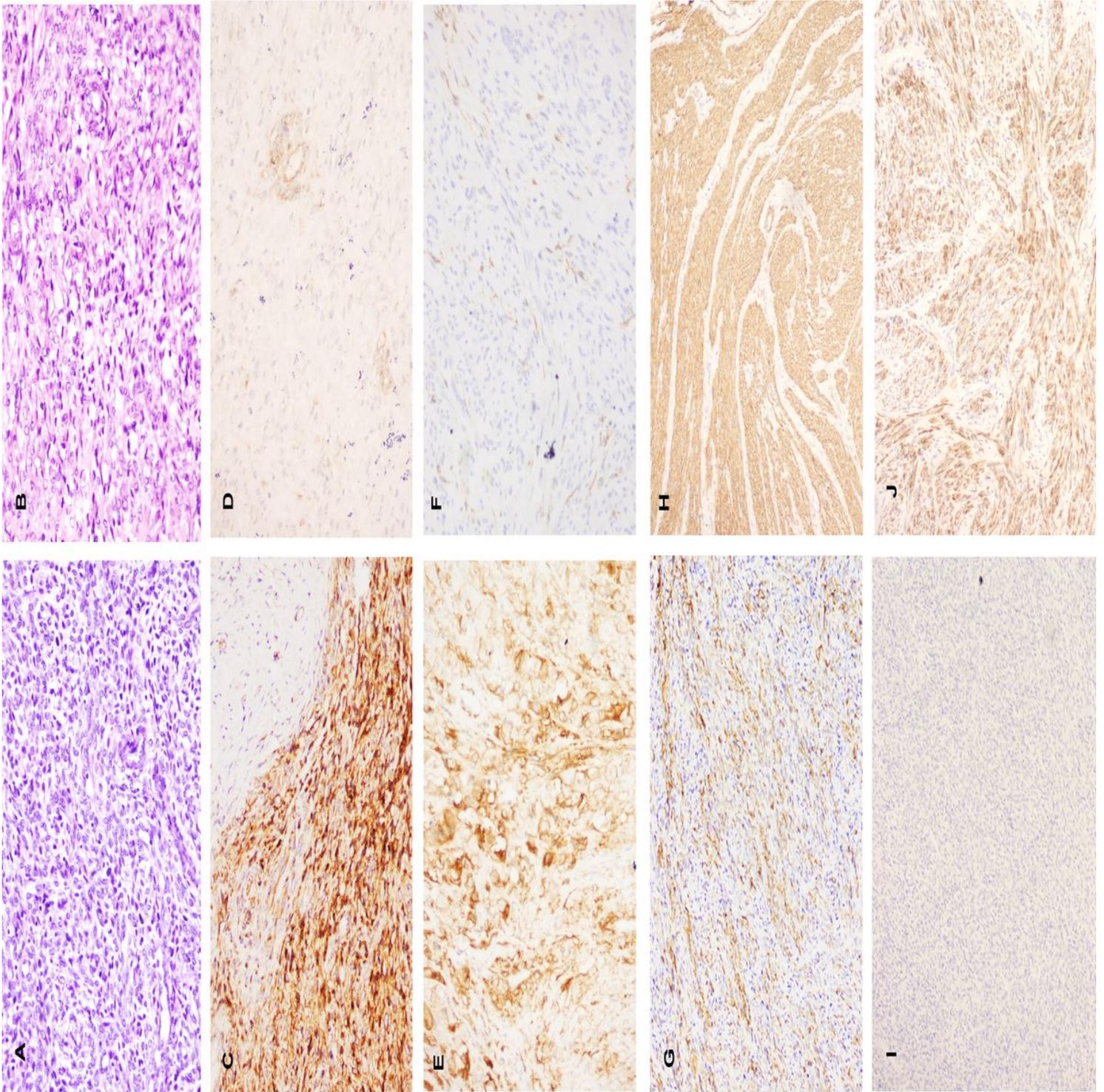


Figure 1

Immunohistochemical results. (A) Endometrial stromal sarcomas (hematoxylin and eosin stains, magnification 200). (B) Cellular leiomyomas (hematoxylin and eosin stains, magnification $\times 200$). (C) Endometrial stromal sarcomas showing strong positive results for IFITM1. (D) Cellular leiomyomas showing a negative or weak expression of IFITM1. (E) Endometrial stromal sarcomas exhibiting a positive expression of CD10. (F) Cellular leiomyomas exhibiting a weekly CD10 positivity. (G) Endometrial stromal sarcomas demonstrating SMA reactivity. (H) Cellular leiomyomas showing strong positive results for

SMA. (I) Endometrial stromal sarcomas showing a negative or weak expression of h-caldesmon. (J) Cellular leiomyomas demonstrating strong positive results for h-caldesmon.

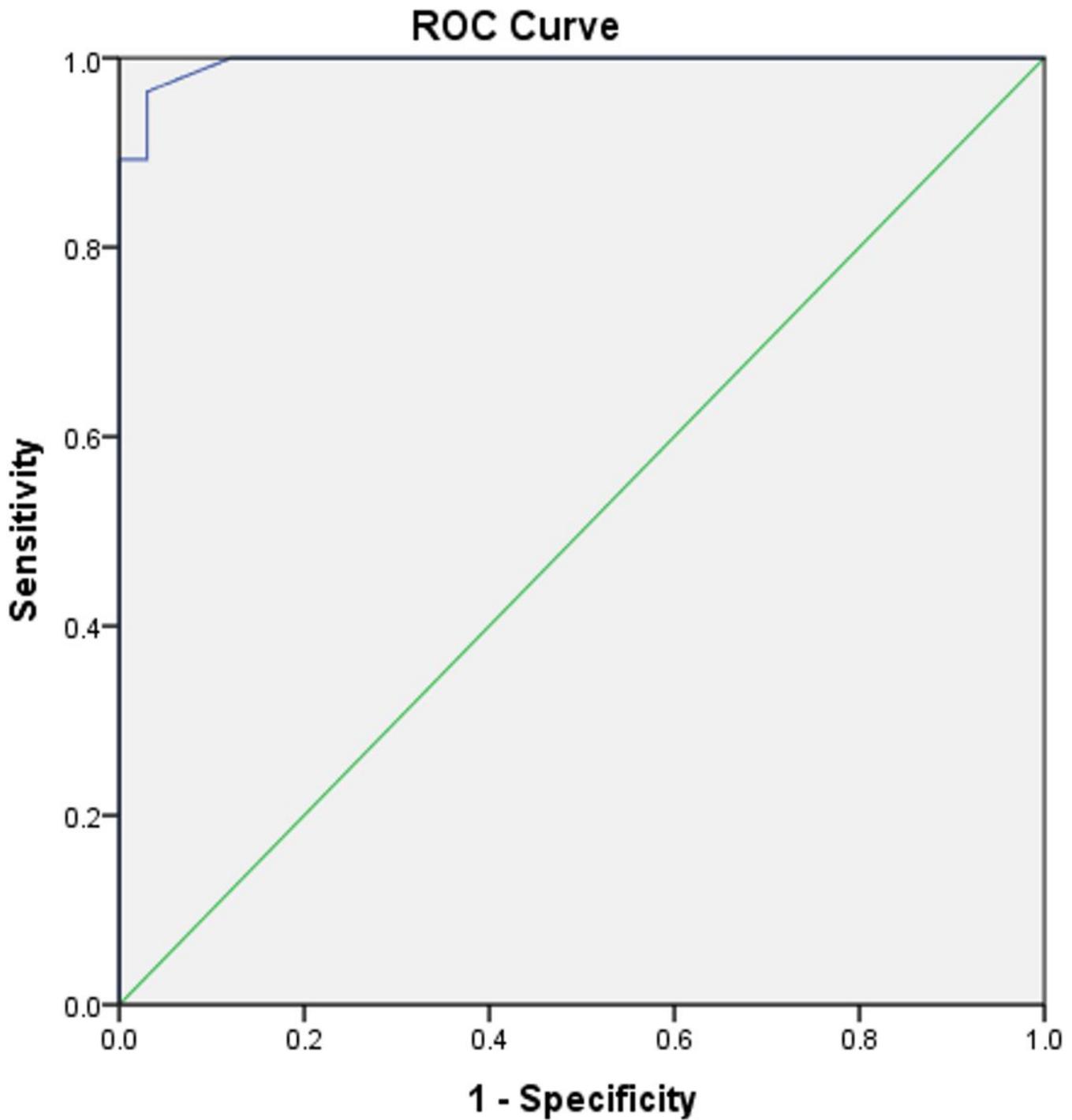


Figure 2

Receiver operating characteristic curve for prediction of Endometrial stromal sarcoma and cellular leiomyoma.

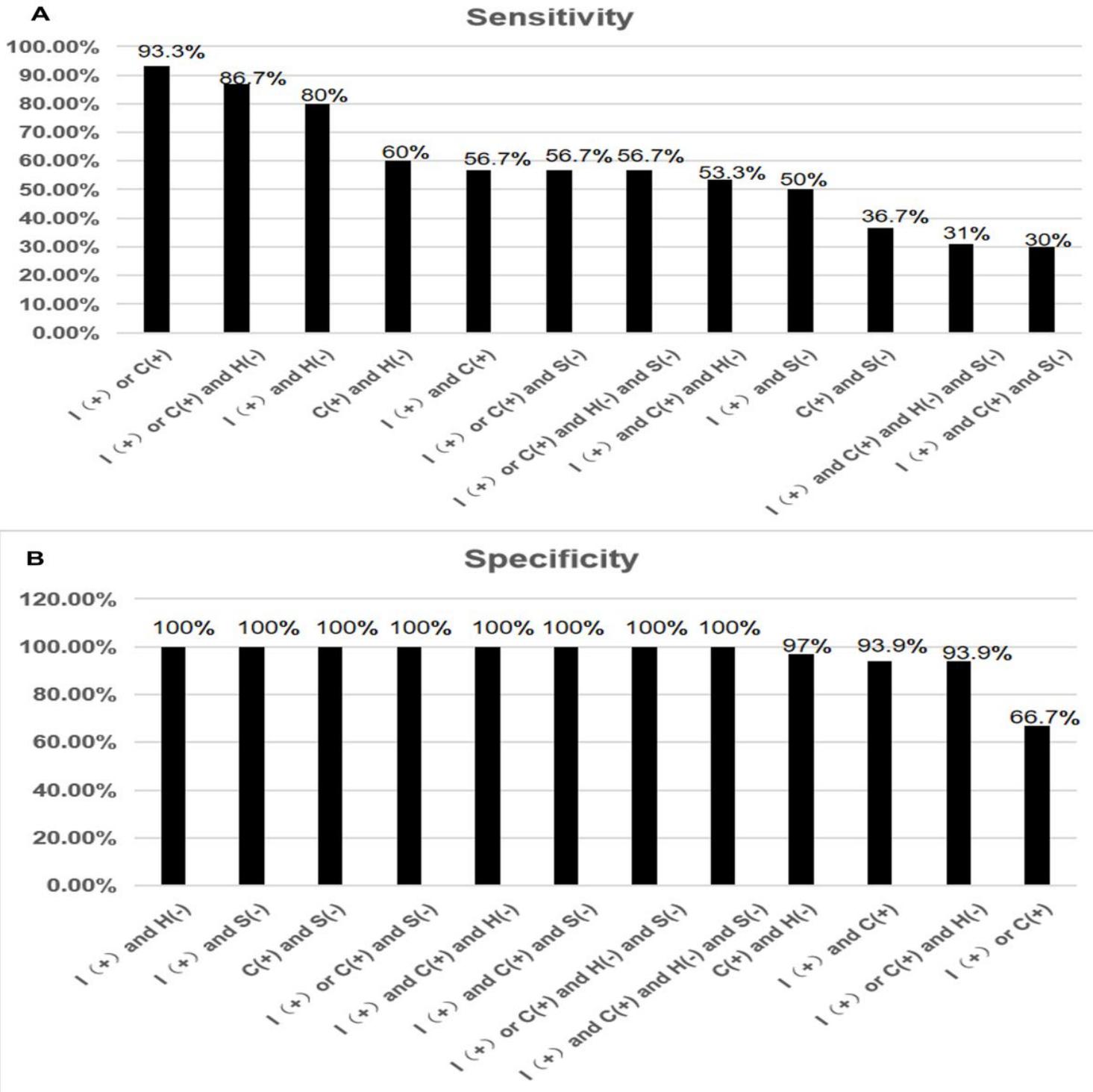


Figure 3

The Sensitivity and Specificity of combined IFITM1,CD10,h-caldesmon and SMA immunostaining in the Diagnosis of endometrial stromal sarcoma. (A) The Sensitivity of different combinations for endometrial stromal sarcoma. (B) The Specificity of different combinations for endometrial stromal sarcoma. Abbreviations: I indicates IFITM1, C indicates CD10, H indicates h-caldesmon, S indicates SMA.

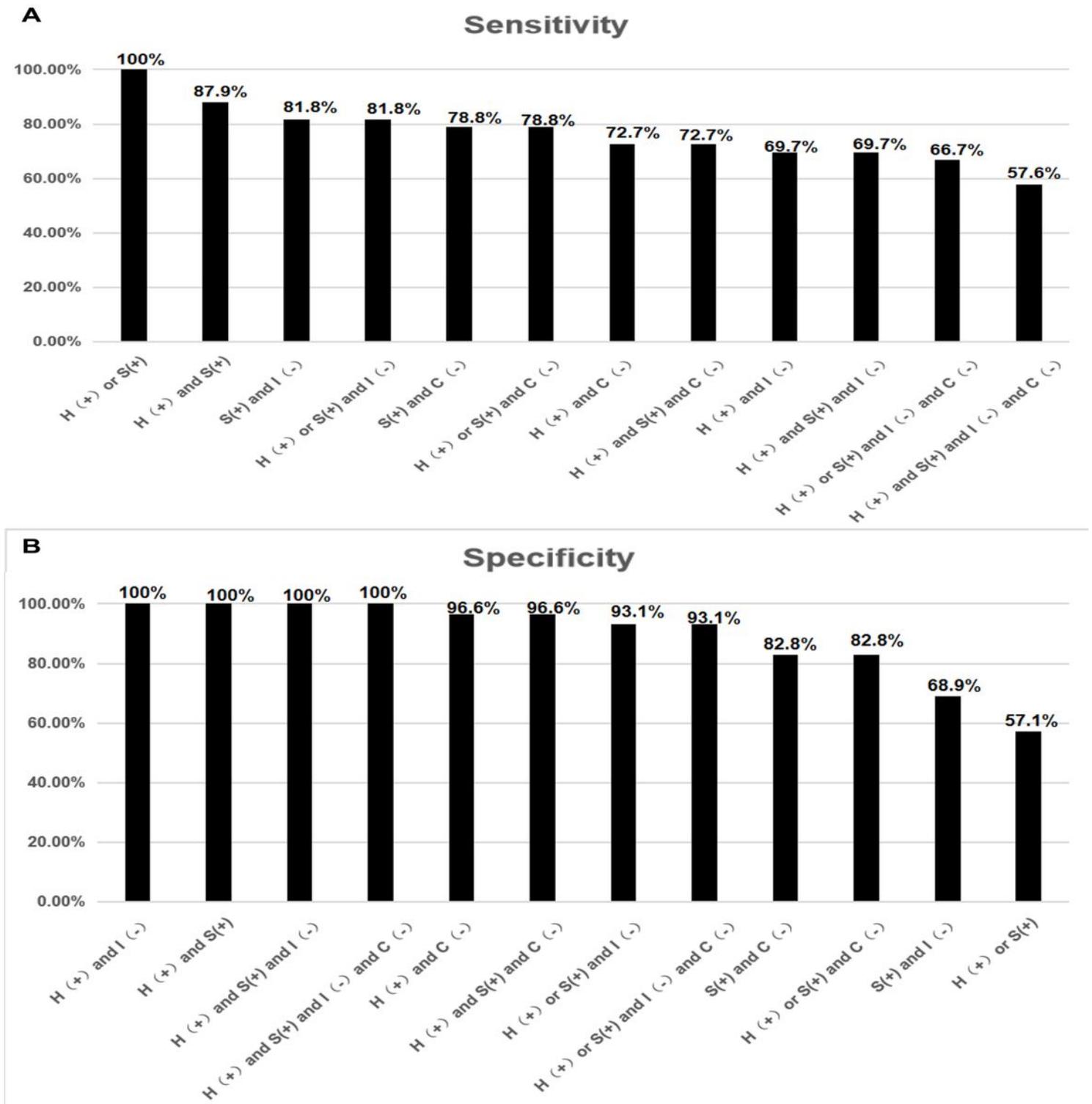


Figure 4

The Sensitivity and Specificity of combined IFITM1,CD10,h-caldesmon and SMA immunostaining in the Diagnosis of cellular leiomyoma. (A) The Sensitivity of different combinations for cellular leiomyoma. (B) The Specificity of different combinations for cellular leiomyoma. Abbreviations: I indicates IFITM1, C indicates CD10, H indicates h-caldesmon, S indicates SMA.