Global *Journal of Imaging and Interventional Medicine*
2021; 2(1): 19-25.
ISSN Online: 2766-9068; ISSN Print: 2766-9076
Website: http://natureschol ars.com
Email: Glo_J_Iim@126.com
Publisher: Scholars Publishing, LLC

Review

Progress in Ultrasonic Diagnosis of Cesarean Scar Pregnancy

Liye Fu[1,2,*], Jinbai Huang[1,3,*,✉]

[1]Medical Imaging Department, Medical College of Yangtze University, Jingzhou, Hubei 434023, China; [2]Changsha Hospital for Maternal and Child Health Care, Changsha, Hunan 410007, China; [3]The First Affiliated Hospital of Yangtze University, Jingzhou, Hubei 434023, China.

*** These authors contributed equally.**

✉ **Correspondence**
Jinbai Huang, Medical Imaging Department, Medical College of Yangtze University, Jingzhou, Hubei 434023, China or The First Affiliated Hospital of Yangtze University, Jingzhou, Hubei 434023, China. Email: jinbaihuang@126.com. Telephone number: 18972161301.

Received: July 27, 2020; Accepted: February 17, 2021; Published: March 31, 2021.
Cite this paper: Fu, L.Y. and Huang, J.B. (2021) Progress in ultrasonic diagnosis of cesarean scar pregnancy. *Global Journal of Imaging and Interventional Medicine*, 2(1): 19-25. http://natureschol ars.com/gjiim.020103. https://doi.org/10.46633/gjiim.020103.

Abstract

Cesarean scar pregnancy (CSP) can lead to severe pregnancy complications. Ultrasound examination is the main method of early diagnosis of CSP, including two-dimensional color/power Doppler ultrasound, three-dimensional color/power Doppler ultrasound, and contrast-enhanced ultrasound. Different ultrasonic techniques have their own characteristics. Ultrasound signs and indicators can predict the outcome of CSP and guide the clinical treatment strategies for CSP patients.

Key words: Cesarean Scar Pregnancy; Ultrasonography; Prognosis.

1. Introduction

Cesarean scar pregnancy (CSP) is a long-term complication of cesarean section. The incidence of CSP is about 0.50‰～0.55‰ (1), in women with a history of cesarean section, which is higher than that of those who underwent a cervical pregnancy. Serious pregnancy complications may occur if the gestation sac attaches to the incision site of the uterus. This may lead to massive bleeding during uterine curettage or pregnancy, which may result in endangering the life of the patient or make the patient lose fertility functions. Therefore, CSP should be correctly diagnosed and treated as soon as possible. Ultrasound examination is of great significance in early diagnosis, risk assessment and clinical treatment of CSP. The commonly-used clinical method is transvaginal two-dimensional color/power Doppler ultrasound (2D-US), and with this technique, the accuracy of detection in early pregnancy is high, at around 84.6% (2). Other auxiliary examinations, such as magnetic resonance imaging (MRI), laparoscopy and hysteroscopy, are available for cases that pose difficult for the transvaginal two-dimensional color/power Doppler ultrasound.

CSP patients often have a history of cesarean section in the lower uterine segment. They visited the hospital with symptoms of menopause, irregular vaginal bleeding, and/or painless or mild abdominal pain. The clinical manifestations lack characteristic symptoms, like ectopic pregnancy or spontaneous abortion, and a few asymptomatic patients are found occasionally in routine examinations. A sudden abdominal pain with severe vaginal bleeding indicates a rupture of the

uterus. Uterine morphology is normal in the early stage. However, the lower segment of the uterus gradually widens or bulges outward with the prolongation of menopause. No mass was found in the bilateral adnexal area, and the uterus was relatively soft on palpation in the case of uterine rupture.

The etiology of CSP is still unclear. The main cause of CSP was thought to be local defect formation resulting from poor cicatrization of the incision site. The surgical method utilized was also related to CSP occurrence. Some studies showed that the breech presentation cesarean section method may increase CSP occurrence due to the poor formation of the lower uterus segment following the procedure, and afterwards, there may be poor incision healing, with uneven thickness of the myometrium.

The surgical suture method utilized may also be associated with the genesis of CSP. It was proven that a single-layer continuous without reverse suture at the incision point in a lower segment cesarean section can easily to contribute poor incision healing, whereas a double-layer with reverse suture in the second layer can reduce the likelihood of CSP. Damage to the endometrium caused by myomectomy, infection, and intrauterine manipulations can also lead to CSP. In these conditions, the muscularis tissue of the incision site could gradually become thin or defective due to local defects of the decidua, a lack of blood supply, and villi tissue invading the lower uterine segment incision, absorbing vital nutrients.

Fibrous connective tissue is formed after the scar tissue is healed at the incision site and this reduces the patient's contraction abilities. When curettage for CSP or miscarriages occur, blood sinuses, which are not able to properly constrict, open and may cause massive bleeding, endangering the life of the patient.

Plenty of literature demonstrated that CSP and morbidly adherent placenta (MAP) had the same histopathological features (3,4). Both have villi tissue planted in the myometrium or around the scar tissue. Due to the decidual defects, the villi tissue penetrated between the muscularis fibers and sometimes invaded the uterine serosal layer or bladder. The effect of local hypoxic tension was considered an important reason for trophoblast cell proliferation and the regulation of placental growth and structure. The scar with implanted villi showed low oxygen tension, which stimulated trophoblast cells to penetrate the scar. MAP could be divided into three types according to the degree of villi invading the myometrium and uterine serosa. In the case of the villi crossing the decidual baseline to reach the myometrium, it was deemed placental accrete; When the villi invaded the deep areas of the myometrium, it was called placenta increta; When the placenta penetrated the myometrium and invades the parietal tissue or the wall of the bladder, it was dubbed placenta percreta. Some scholars believed that blastocysts prefer "exposed" scar tissue, that is, tissue stripped of endometrial epithelial cells. Studies have shown that the causes of CSP hemorrhage were neovascularization and significant pelvic adhesions, as well as surgical separation of the uterus from the bladder and parametrium tissue.

The therapeutic methods of CSP include drug, surgical, and expectant treatment (5-8). Drug therapy mainly depends on methotrexate (MTX), which can be used for systemic or local injection, or in combination with KCL or mifepristone. Surgical treatment includes curettage surgery (usually under the guidance of ultrasound), hysteroscopy, laparoscopic, laparotomy, and uterine artery embolization (UAE) and hysterectomy. Some scholars adopted other methods, such as a balloon catheter placed in the uterine cavity, local injection of vasopressin or epinephrine, uterine artery ligation, high-intensity focused ultrasound ablation and so on, to treat or assist in the treatment of this disease. Delayed treatment in CSP patients could lead to placental implantation or uterine rupture, which is difficult to treat and, may lead to massive bleeding and hysterectomy. Expectant treatment means that CSP patients did not use artificial measures to restrict the development of the gestational sac. Instead, expectant treatment (9,10) entails waiting for the gestational sac to continue pregnancy or for spontaneous abortion, dissolution, and absorption to occur. 57 percent of women diagnosed with CSP who refused to terminate their pregnancy with fetal heartbeat in the pregnancy sac gave birth to live fetuses with an average gestational age of 34±3 weeks, but about 63 percent of them required a hysterectomy due to complications. The best treatment for CSP has not been determined. The aim of these treatments was to terminate the pregnancy before the pregnancy sac ruptures, remove the pregnancy capsule, reduce severe complications, and preserve the patient's fertility in the future.

2. Ultrasonic diagnostic technology and its value

Imaging diagnosis techniques of CSP include the two-dimensional color/power Doppler

ultrasound (2D-US), three-dimensional color/power Doppler ultrasound (3D-US), contrast-enhanced ultrasound (CEUS), and MRI. Although the soft tissue and spatial resolution of the MRI has a potential advantage in the diagnosis of CSP, it cannot dynamically observe whether there is a heartbeat in the embryo of the pregnancy sac. Furthermore, the cost of MRI is high, the examination time is long, and the operation is complex. Therefore, the early imaging diagnosis of CSP mainly relies on ultrasound examination.

2.1 Two-dimensional color/power Doppler ultrasound

The two-dimensional color/power Doppler ultrasound has the advantages of simple operation, safety, noninvasion, low cost, and real-time imaging. When the transvaginal ultrasound was performed, the probe was close to the uterus, and the image resolution was high. All these properties easily reveal the relationship between the pregnancy sac and the incision site. On the other hand, transabdominal ultrasounds can show the relationship between the pregnancy sac or mass and the bladder from an overall perspective. Color Doppler flow imaging (CDFI) can assess blood supply around the pregnancy sac, measure blood flow velocity, and evaluate the resistance index. The transvaginal two-dimensional color/power Doppler ultrasound and transabdominal two-dimensional color/power Doppler ultrasound can be used in combination to complement one another.

2.2 Three-dimensional color/power Doppler ultrasound

The three-dimensional color/power Doppler ultrasound can display the transverse, sagittal, and coronal planes of the uterus at the same time. In contrast, the ability of the traditional two-dimensional color/power Doppler ultrasound to display the coronal plane is limited. Three-dimensional doppler ultrasounds can display the position and geometry of the pregnancy sac with a steric image, which can show the interface between the bladder and the thin anterior myometrium of the uterus in a descriptive, informative picture and improve the detection rate of CSP in early pregnancy. The two-dimensional color/power Doppler ultrasound can easily lead to misdiagnosis when the blood flow velocity of the lesion is low. The three-dimensional color/power Doppler ultrasound can show the relationship between the lesion, incision, and blood flow signals around it in multiple planes, providing increased anatomical detail, which is a beneficial supplement to the two-dimensional color/power Doppler ultrasound (11,12).

2.3 Contrast-enhanced ultrasound

The contrast-enhanced ultrasound (CEUS) is a new type of ultrasound diagnostic technique. The target area is examined by ultrasound at the same time as the intravenous injection of an ultrasound contrast agent, a blood pool contrast agent, consisting of phospholipid-stabilized shell microbubbles filled with sulfur hexafluoride gas. The contrast agent can enhance the backscattered echoes and be excreted through the respiratory system with no nephrotoxicity and no necessary allergy tests. This agent can significantly improve the ultrasonic resolution, sensitivity, and specificity, and it can be traced in real time. The normal uterus is gradually intensified from the serosa to the endometrium, and the pregnancy sac in the normal position is implanted in the endometrium. The time it takes for the ultrasound contrast agent to reach the pregnancy sac should be later than it reaches the serosa. However, the time for the ultrasound contrast agent to reach the pregnancy sac in CSP patients is earlier than the time to reach the serosa of the uterus, showing the characteristics of rapid enhancement and slow fading (11). CEUS can show the uterine boundary more clearly and can directly observe whether there is any overflow of contrast agent between the lesion and bladder, providing more reliable evidence to judge the continuity of the myometrium and the serosal. CEUS is superior to the two-dimensional color/power Doppler ultrasound in image resolution, display of small blood vessels, and depiction of low-speed blood flow. Ultimately, this technique is an important supplementary method for the two-dimensional color/power Doppler ultrasound (13).

3. Ultrasonic diagnostic criteria and image classification

The criteria of ultrasonic diagnosis of CSP are as follows (2,3,14,15): 1. Presence of a pregnancy sac with or without fetal heart activity; 2. Complete or partial implantation of the pregnancy sac can be seen in the scar of the anterior wall of the uterus, or mixed echo mass can be seen in the incision of the uterus; 3. The myometrium between the bladder and the pregnancy sac is thin or indistinct and defective; 4.

Part or none of the pregnancy sac is found in the uterine cavity and cervical canal, and the cervical canal is closed; 5. Before 8 weeks of pregnancy, the edge of the pregnancy sac near the incision is sharp, and after 8 weeks of pregnancy, the shape of the pregnancy sac may be round; 6. Abundant blood perfusion was observed in the pregnancy sac, and the blood flow signals can be seen from the incision. Color/power Doppler ultrasounds can effectively assess the blood supply of the pregnancy sac or mass and draw the outline of the CSP masses. Typical CSP shows high speed and low impedance blood flow. Not all of the above indicators can be shown under ultrasound, especially when the gestational weeks are small, or the ultrasound was performed before the emergence of heart activity in the pregnancy sac.

According to the different echo of the lesion, ultrasonic image classification can be divided into two types: pregnancy sac type and heterogeneous mixed echo mass type. According to the location of the lesion, CSP can be divided into partial and complete CSP, also known as endogenous and exogenous (5,16), respectively. During partial CSP, part of the lesion is in the uterine cavity and part is implanted in the scar of the uterus. The pregnancy sac grows toward the uterine cavity. In a complete incisional pregnancy, the pregnancy sac is completely implanted in the scar of the uterus and grows toward the bladder.

CSP was divided into three types by experts from the society of obstetrics and gynecology at the Chinese Medical Association according to the implantation site, growth direction, and the thickness of the tissue between the lesion and the bladder (13). Type I and type II are equivalent to partial CSP, and the lesion is partially implanted in the scar of the uterus and grows toward the uterine cavity. For type I, the thickness between the lesion and the bladder tissue was greater than 3mm, while for type II, the thickness between the lesion and the bladder tissue was less than or equal to 3mm and the blood flow signal of low resistance nourishing blood vessels can be detected by color/power Doppler ultrasound. Type III is equivalent to a complete CSP. In type III, the lesion was completely implanted in the scar of the anterior wall and expanded toward the bladder. The thickness of the tissue between the lesion and the bladder is less than or equal to 3mm and the lesion is detected through the color/power of the Doppler ultrasound, with blood flow signals of low resistance nourishing blood vessels, and an empty uterine cavity and cervical canal.

It is difficult to distinguish CSP from intrauterine pregnancy when most of the pregnancy sac is located above the level of uterine incision and only a small part of the pregnancy sac reaches the scar (11). Timet al. (17) presented a method for identifying CSP and intrauterine pregnancy between 5 and 10 weeks of gestation. According to their study, a straight line is drawn between the uterine fundus and the external os of the cervix. The midpoint on this line was considered the midpoint of the uterus. They pointed out that most of the CSPs were located closer to the midpoint of the uterus, while the intrauterine pregnancy sac was located further away from the midpoint of the uterus. However, the study did not suggest how far the distance between the pregnancy sac and the midpoint of the uterus would be to distinguish between CSP and intrauterine pregnancy. They also pointed out that the final diagnosis of CSP still needed to be combined with clinical and ultrasonic diagnostic criteria.

4. Prognostic indicators of ultrasonic diagnosis

Pregnant women with partial CSP may continue to gestation into the third trimester, but there is a risk of massive bleeding or uterine rupture. Pregnant women with complete CSP may experience massive bleeding or uterine rupture in the early period of gestation(11). Some scholars proposed a new sonographic sign that can predict adverse pregnancy outcomes in early pregnancy for patients with CSP, namely the crossover sign (COS). In their study, after the diagnosis of CSP, a line was drawn between the uterine fundus and the internal cervical os, in the sagittal plane of the uterus. This line crossed the endometrium and is assumed to be the endometrial line. Perpendicular to the endometrial line, the superior–inferior (S–I) diameter of the pregnancy sac was drawn. According to the relationship between the S-I diameter of the pregnancy sac and the endometrial line, patients were divided into two groups : (1) COS-1, in which more than 2/3 of the S-l diameter of the pregnant sac was located above the endometrial line; (2) COS-2, in which not more than 2/3 of the S-l diameter of the pregnant sac was located above the endometrial line. These patients were further subdivided into two categories: those with the (COS-2+) intersection of the S–I diameter of the pregnant sac with the endometrial line present and those with the (COS-2–) intersection of the S–I diameter of the pregnant sac with the endometrial line absent. Their study found that pregnant women in the COS-1 group had shorter gestational weeks than

those in the COS-2 group, and pregnant women in the COS-1 group were more likely to have placenta percreta and increta, suggesting that they had a higher risk of invading the bladder and surrounding tissues of the uterus, massive bleeding, and intraoperative complications, while pregnant women in the COS-2 group were more likely to have the mild form of MAP, such as the placenta accreta (18,19).

Some scholars have proposed that cases of CSP with fetal heartbeat present in the pregnancy sac are at higher risk of serious obstetrics and gynecology complications (such as massive hemorrhage, uterine rupture in early pregnancy, hysterectomy, and severe MAP) after expectant treatments. The risk of uterine rupture and hysterectomy during early pregnancy is negligible for cases of CSP without fetal heartbeat present in the pregnancy sac (3).

Kaelin Agten et al (1). considered that implantation of the pregnancy sac "on the scar" has a better prognosis than implantation of the pregnancy sac " in the niche". "On the scar" was defined as the placenta being partially or completely planted on the surface of a well healed incision, while " in the niche" was defined as the placenta being planted into a deficient or dehiscent scar. Expectant treatment may be considered if the pregnant women with CSPs implanted "on the scar" and the thickness of the anterior wall of the uterus is equal to or greater than 4mm. Termination of pregnancy is not the only correct option.

5. Selection of CSP treatment

The treatment of CSP mainly depends on clinical symptoms, gestational weeks, fertility requirements, morphological characteristics of the uterine placental neovascularization, and the patient's own wishes. When the myometrium thickness of the anterior wall of the uterus is less than 2mm, the risk of uterine rupture is high, so a hysteroscopy is not a suitable treatment, but a laparotomy or a pharmaceutical treatment can be used. The endogenous CSP is more likely to be completely cleared during curettage, while the exogenous CSP grows toward the bladder or abdominal cavity, which is difficult to be cleared by curettage and has a relatively high risk of bleeding. Therefore, attention should be paid to the ultrasonic image characteristics during treatment. Some scholars believe that evaluating the morphological characteristics of uterine placental neovascularization is the most important factor in determining the treatment. Compared with the traditional two-dimensional color/power Doppler ultrasound, a three-dimensional color/power Doppler ultrasound and CEUS examination can better reflect the lesion's blood flow. If blood flow or lesion enhancement is still present on the imaging results after terminating the pregnancy, indicating that the lesion still has viable villi tissue, additional treatment may be considered. Both methods can be used to evaluate the therapeutic effect (20). When blood supply is rich, it may lead to complex and massive hemorrhage, and uterine artery embolization is an important treatment. The increased blood flow, large volume of the lesion, and existence of embryonic heartbeat all serve to increase the rate of treatment failure. Ultrasound examination can objectively indicate the size of residual lesions, display the range of blood supply and the vascular resistance, and determine the heartbeat of the embryo, providing important information for clinical treatment selection, therapeutic effect evaluation, and judgment on whether additional treatment is needed.

In general, the early diagnosis of CSP mainly relied on two-dimensional color/power Doppler ultrasounds. For patients with unclear diagnoses and whose situations indicate difficulty in judging blood supply, three-dimensional color/power Doppler ultrasounds, CEUS, and other auxiliary examinations can be used in combination. Corresponding treatment measures can be given according to different types of CSP, and prognostic indicators as suggested by the ultrasound.

Serious complications, such as massive hemorrhage, hysterectomy due to uterine rupture, and even mortality, often led to the decision to terminate the pregnancy early. In fact, the early termination of the pregnancy is a common clinical practice, but many older women or women who have difficulties with pregnancies are eager to continue their pregnancies with expectant treatments. How to determine which woman with CSP displays the conditions that indicate a minimal risk of complications and is suitable to continue the pregnancy? At its current stage, we conclude that ultrasonic examination technology still requires more exploration and research to effectively answer that question.

Declarations

1) ***Consent to publication***
We declare that all authors agreed to publish the manuscript at this journal based on the signed Copyright Transfer Agreement and followed publication ethics.

2) Ethical approval and consent to participants
Not applicable.

3) *Disclosure of conflict of interests*
We declare that no conflict of interest exists.

4) Funding
None

5) Availability of data and material
We declare that the data supporting the results reported in the article are available in the published article.

6) Authors' Contributions
7) Authors contributed to this paper with the design (LYF), literature search (LYF), drafting (LYF), revision (LYF and JBH), editing (LYF and JBH) and final approval (JBH).

8) *Acknowledgement*
None

9) Authors' biography
None

References

1. Kaelin Agten A, Cali G, Monteagudo A, Oviedo J, Ramos J, Timor-Tritsch I. The clinical outcome of cesarean scar pregnancies implanted "on the scar" versus "in the niche". Am J Obstet Gynecol. 2017;216(5):510.e1-6.
2. Miller R, Timor-Tritsch IE, Gyamfi-Bannerman C. Society for Maternal-Fetal Medicine (SMFM) Consult Series #49: Cesarean scar pregnancy. Am J Obstet Gynecol. 2020;222(5):B2-14.
3. Calì G, Timor-Tritsch IE, Palacios-Jaraquemada J, Monteaugudo A, Buca D, Forlani F, et al. Outcome of Cesarean scar pregnancy managed expectantly: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2018;51(2):169-75.
4. D'antonio F, Timor-Tritsch IE, Palacios-Jaraquemada J, Monteagudo A, Buca D, Forlani F, et al. First-trimester detection of abnormally invasive placenta in high-risk women: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2018;51(2):176-83.
5. Maheux-Lacroix S, Li F, Bujold E, Nesbitt-Hawes E, Deans R, Abbott J. Cesarean Scar Pregnancies: A Systematic Review of Treatment Options. J Minim Invasive Gynecol. 2017;24(6):915-25.
6. Timor-Tritsch IE, Monteagudo A, Bennett TA, Foley C, Ramos J, Kaelin Agten A. A new minimally invasive treatment for cesarean scar pregnancy and cervical pregnancy. Am J Obstet Gynecol. 2016;215(3):351.e1-8.
7. Timor-Tritsch IE, Khatib N, Monteagudo A, Ramos J, Berg R, Kovács S. Cesarean scar pregnancies: experience of 60 cases. J Ultrasound Med. 2015;34(4):601-10.
8. Birch Petersen K, Hoffmann E, Rifbjerg Larsen C, Svarre Nielsen H. Cesarean scar pregnancy: a systematic review of treatment studies. Fertil Steril. 2016;105(4):958-67.
9. Jayaram P, Okunoye G, Al Ibrahim AA, Ghani R, Kalache K. Expectant management of caesarean scar ectopic pregnancy: a systematic review. J Perinat Med. 2018;46(4):365-72.
10. Vikhareva O, Nedopekina E, Herbst A. Normal vaginal delivery at term after expectant management of heterotopic caesarean scar pregnancy: a case report. J Med Case Rep. 2018;12(1):179.
11. Liu D, Yang M, Wu Q. Application of ultrasonography in the diagnosis and treatment of cesarean scar pregnancy. Clin Chim Acta. 2018;486:291-7.
12. Shao MM, Cai AL, Wang XG, Sun W, Wang B, Sun L. Three-dimensional tomographic ultrasound imaging in diagnosis of the cesarean scar pregnancy. Chin J Med Imaging Technol. 2015;31(06):893-6.
13. Wu Y, Zhou L, Chen L, Zhou Q, Zeng T. Efficacy of contrast-enhanced ultrasound for diagnosis of cesarean scar pregnancy type. Medicine (Baltimore). 2019;98(44):e17741.
14. D'antonio F, Palacios-Jaraquemada J, Lim PS, Forlani F, Lanzone A, Timor-Tritsch I, et al. Counseling in fetal medicine: evidence-based answers to clinical questions on morbidly adherent placenta. Ultrasound Obstet Gynecol. 2016;47(3):290-301.
15. Grechukhina O, Deshmukh U, Fan L, Kohari K, Abdel-Razeq S, Bahtiyar MO, et al. Cesarean Scar Pregnancy, Incidence, and Recurrence: Five-Year Experience at a Single Tertiary Care Referral Center. Obstet Gynecol. 2018;132(5):1285-95.
16. Gonzalez N, Tulandi T. Cesarean Scar Pregnancy: A Systematic Review. J Minim Invasive Gynecol. 2017;24(5):731-8.
17. Timor-Tritsch IE, Monteagudo A, Cali G, El Refaey H, Kaelin Agten A, Arslan AA. Easy sonographic differential diagnosis between intrauterine pregnancy and cesarean delivery scar pregnancy in the early first trimester. Am J Obstet Gynecol. 2016;215(2):225.e1-7.
18. Calì G, Forlani F, Minneci G, Foti F, Di Liberto S, Familiari A, et al. First-trimester prediction of surgical outcome in abnormally invasive placenta using the cross-over sign.

Ultrasound Obstet Gynecol. 2018;51(2):184-8.
19. Cali G, Forlani F, Timor-Tritsch IE, Palacios-Jaraquemada J, Minneci G, D'antonio F. Natural history of Cesarean scar pregnancy on prenatal ultrasound: the crossover sign. Ultrasound Obstet Gynecol. 2017;50(1):100-4.
20. Liu D, Gu X, Liu F, Shi F, Yang M, Wu Q. Application of contrast-enhanced ultrasound for scar pregnancy cases misdiagnosed as other diseases. Clin Chim Acta. 2019;496:134-9.