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弱精症不育患者睾丸相关指标与精索静脉曲张超声检查关系的探讨

叶 磊,隋秀芳,王 磊,张敬安,叶显俊

摘要 对129例弱精症患者[伴精索静脉曲张(VC)113例]与30例正常对照者进行彩超检查,主要检查睾丸、附睾、精索静脉最大内径及精索静脉返流情况,将113例精索静脉曲张患者设为曲张组,并进行超声分级,分为亚临床型精索静脉曲张(SVC)、临床型精索静脉曲张(VC1、VC2、VC3)。比较组间睾丸体积、精液质量变化的差异性,以及曲张组内两两组间睾丸体积及精液质量变化的差异性。组间差异有统计学意义,曲张组左侧睾丸平均体积小于正常组左侧睾丸平均体积($P<0.01$);曲张组内左侧睾丸平均体积均明显小于同级右侧睾丸平均体积($P<0.05$),VC2、VC3两组右侧睾丸体积均明显小于正常组右侧睾丸体积($P<0.05$),VC3组的右侧睾丸体积小于SVC组($P<0.05$)。曲张组的精液质量(精子活力、精子活率及精子密度)均明显低于正常对照组($P<0.01$);VC组内两两比较差异均有统计学意义($P<0.05$)。VC可引起睾丸体积减小,精液质量下降,随曲张程度增加,睾丸体积变小越明显、精液质量的变化也呈下降趋势。

关键词 弱精症;精索静脉曲张;睾丸体积;精液质量;超声

中图分类号 R 445.1;R 698+,2

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近年男性不育患者不断增加,不育原因有很多,WHO将精索静脉曲张(varicocele,VC)列为青壮年男性不育原因的首位,可见其在男性不育中的重要地位。超声检查VC作为一种实时、无创、方便以及更加价廉的方法被广泛应用于临床。超声检查能准确测量睾丸大小、精索静脉最大内径、清晰显示精索静脉血流情况等相关信息,该研究旨在探讨VC的超声检查与睾丸相关指标(睾丸体积及精液质量)之间的关系。

1 材料与方法

1.1 病例资料 选取2013年10月~2014年7月,我院门诊经精液常规检查证实为弱精症129例,并经超声诊断为VC的113例患者作为曲张组。入选条件:① 经超声诊断为左侧VC的弱精不育症患者;② 该组患者中除左侧VC外,无生殖系统感染、睾丸发育异常及无精症等其他影响精子质量导致弱精症的因素。选取2013年10月~2014年7月经超声检查无VC及精液常规检查均正常的已婚已育男性30例作为正常对照组,年龄23~36(26.0±3.4)岁。

1.2 实验器材 采用飞利浦HD15彩色超声诊断仪,探头频率5~12 MHz。

1.3 方法 患者仰卧位,将阴茎托起贴于腹壁,检查睾丸、附睾及精索静脉,测量并计算睾丸体积,睾丸体积计算公式为长(mm)×高(mm)×宽(mm)×0.71÷1 000(ml)。测量左侧精索静脉平静时及Valsalva实验时的最大内径,彩色多普勒观察血流及观察返流情况。留取曲张组、正常对照组精液常规检查结果(主要记录精子活力、精子活动率及精子密度值)。VC超声分级标准[1]:分亚临床型精索静脉曲张(subclinical varicocele,SVC)及临床型VC。SVC:临床触诊阴性,内径1.8~2.1 mm,平静呼吸

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difference in diagnostic accuracy of tumor size assessment between ultrasonography and pathological examination. The size, contour, border, liquefactive necrosis were markedly correlated with the patholobiologic behavior of tumors($P<0.01$). The ultrasonography features of high-risk GIST: size, larger than 5 cm, irregular shape, poor-defined boundary. It could improve the sonographic diagnosis of gastrointestinal stromal tumor through drinking water. The positioning accuracy of GIST with fasting was significantly lower than that of after drinking water($P<0.01$).

Key words ultrasonography; gastrointestinal stromal tumor

无返流，Valsalva 试验静脉偶见返流；VC：1 级：临床触诊阳性，内径 2.2 ~ 2.5 mm，平静呼吸无返流，Valsalva 试验静脉有短暂返流；2 级：临床触诊阳性，内径 2.6 ~ 3.0 mm，平静呼吸有短暂返流，Valsalva 试验静脉有持续返流；3 级：临床触诊阳性，内径 > 3.0 mm，平静呼吸有持续的返流，Valsalva 试验静脉返流明显增强。Valsalva 实验，即深吸气后，在屏气状态下用力作呼气动作，并记录所测值。见图 1。

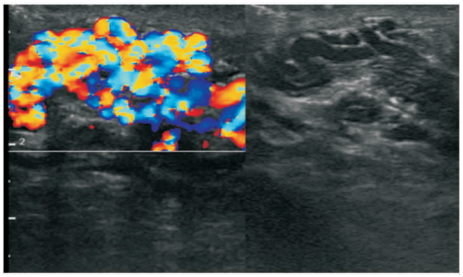

图 1 VC3 级 Valsalva 试验彩超表现

1.4 统计学处理 采用 SPSS 16.0 统计分析软件处理，计量资料以 $\bar{x} \pm s$ 表示，左侧与右侧体积均数比较运用两独立样本 t 检验；组间比较运用单因素方差分析，两两比较运用 SNK-q 法。

2 结果

曲张组左侧睾丸平均体积小于正常对照组左侧睾丸平均体积（$F = 18.83$、10.48，$P < 0.01$），见表 1。曲张组每组左侧睾丸平均体积均明显小于右侧睾丸平均体积（$P < 0.05$），VC2、VC3 两组右侧睾丸体积均明显小于正常对照组右侧睾丸体积（$P < 0.05$），VC3 组的右侧睾丸体积小于 SVC 组（$P < 0.05$）。曲张组的精子活力、精子活率及精子密度均明显低于正常对照组（$F = 17.08$、112.90、13.08，$P < 0.01$），见表 2。VC 组内两两比较差异均有统计学意义（$P < 0.05$），随曲张程度增加，睾丸体积越小、精子质量越差。见图 2。VC2 及 VC3 组中左侧 VC，双侧睾丸体积明显减小。

表 1 VC 各组与正常对照组双侧睾丸体积的比较（$\bar{x} \pm s$）

组别	n	睾丸体积（ml）	
		左侧	右侧
正常对照	30	13.22 ± 1.51	13.27 ± 1.35
SVC	27	12.17 ± 1.01$^{**\#}$	12.96 ± 0.96
VC1	28	11.13 ± 1.63$^{**\#}$	11.85 ± 1.26
VC2	33	10.52 ± 1.98$^{**\#}$	11.46 ± 2.14*
VC3	25	9.85 ± 1.85$^{**\#\blacktriangle}$	11.28 ± 1.77*

与正常对照组比较：$^{*}P < 0.05$，$^{**}P < 0.01$；与右侧比较：$^{\#}P < 0.05$；与 SVC 组比较：$^{\blacktriangle}P < 0.05$

表 2 正常对照组与 VC 各组精子活力、精子活率及精子密度的比较（$\bar{x} \pm s$）

组别	精子活力（%）	精子活率（%）	精子密度（$\times 10^6$/ml）
正常对照	62.87 ± 10.13	75.12 ± 15.37	65.15 ± 23.51
SVC	51.48 ± 17.76**	40.48 ± 10.76**	51.24 ± 25.43*
VC1	45.16 ± 20.08**	32.37 ± 11.25**	41.38 ± 23.19**
VC2	39.54 ± 19.92**	25.52 ± 9.06**	35.15 ± 25.02**
VC3	30.20 ± 12.34**	18.08 ± 7.38**	22.47 ± 19.75$^{**\#}$

与正常对照组比较：$^{*}P < 0.05$，$^{**}P < 0.01$；与 SVC 组比较：$^{\#}P < 0.05$

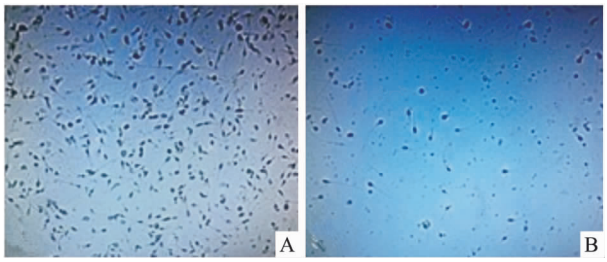

图 2 正常及 VC 的精子轨迹

A：正常者精子轨迹；B：VC3 级精子轨迹

3 讨论

VC 在男性原发性不育中约占 35% ~ 40%，在继发性不育中约占 75% ~ 81%，是男性不育的主要原因[2]。在弱精症不育患者中，VC 发生的比例更高，在本研究中达 87.6%。VC 以左侧居多，主要原因可能是其特殊的解剖位置关系，左侧精索静脉以直角汇入左肾静脉，并且有部分左侧 VC 患者伴有左肾静脉受压，另外长期站立、行走、劳累、久蹲、久坐、饮酒等因素都是常见的导致曲张的原因。

有学者认为 VC 可引起睾丸体积缩小及精液质量下降，本研究结果与之相符[3-4]。可能的主要原因有以下几点：① VC 引起睾丸微循环障碍：VC 时精索静脉瓣功能缺失或功能不全，造成静脉血液返流，使精索静脉内压升高，从而影响睾丸血供，导致精子成熟障碍及精子活力下降。阮衍泰等[5]认为 VC 时睾丸组织发生病理改变，呈“斑点样”表现，即正常生精小管与病变组织交替存在，这种表现可能与睾丸血流重新分布有关。② VC 时肾脏及肾上腺代谢的血管活性物质返流：左侧 VC 时左肾静脉反流的血液将血液内的肾上腺及肾脏代谢产物带入左

侧睾丸,具有毒副作用,造成睾丸损伤。其中对睾丸生精影响较大的主要有5-羟色胺、前列腺素F2α、儿茶酚胺及类固醇等,以5-羟色胺、前列腺素F2α影响最大,有研究[5]表明5-羟色胺对睾丸有毒性作用,前列腺素F2α使睾丸血液循环下降,增加附睾收缩,影响精子成熟及降低精子的活动力,同时能使睾丸睾酮水平降低及睾丸间质细胞分泌减少。③ VC时精索静脉内的一氧化氮(NO)升高[6]:NO对精子功能的影响是双重的,低浓度时对精子功能有保护作用,高浓度时会减少睾丸血供、影响性激素分泌、损害生精过程、降低精子获能和顶体反应率、抑制精子的活动度,导致生育力下降。④ 凋亡机制:近年来生精细胞凋亡异常在VC导致男性不育机制研究上取得重要进展。研究[7-8]显示生精细胞凋亡是VC致生精细胞损害的病理机制,而且与VC的程度密切相关。⑤ 氧化应激机制:VC时活性氧(ROS)过度生成和抗氧化机制缺陷导致氧化应激,这是VC导致不育的重要分子机制[9]。ROS通过启动细胞膜的脂质过氧化致精子形态改变、代谢及功能异常。⑥ 免疫状态不恒定和解剖结构异常也是VC引起生精功能异常的原因。VC时睾丸内静脉压增高,局部代谢产物不易排出,有毒物质的蓄积,血原睾屏障的破坏使免疫复合物在睾丸组织中沉积,使精子释放入血液产生抗精子抗体。⑦ 附睾功能异常:VC可以造成附睾功能异常,影响精子的成熟,从而造成男性生育能力下降。

睾丸体积广泛被认为是反映睾丸生精能力的一项基本指标。由于80%睾丸体积由生精小管组成,睾丸体积减小提示生精功能受损。睾丸体积≤10 ml时,睾丸组织发生病理改变,睾丸引起生精功能障碍[10]。本研究显示随VC程度加重,睾丸体积呈减小趋势,精子质量也呈下降趋势,而且一侧曲张到一定程度可以引起双侧睾丸体积明显缩小,此时对精子质量影响更加明显。可能的原因除上述免疫机制外还可能与左右侧睾丸之间存在丰富的侧枝循环有关[11]。

本研究还显示,SVC同样可以引起睾丸质量下降,SVC的血管内径往往增粗不明显,临床触诊阴性,但早期可以累及血管瓣,使静脉血液返流,同样可以引起睾丸温度上升,局部血液瘀滞及睾丸局部内环境的改变,以致引起生育能力的下降[2]。VC对睾丸损害过程是逐渐发展且进行性加重的,因此,早期诊断VC尤其是SVC是早期治疗的关键。彩超检查简单、无创、重复性好,可对VC分级,对精索静脉血流状态可以直观、准确、清晰的描述,尤其对临床触诊阴性、诊断较难的SVC患者优势明显,具有良好的实用价值[12],同时为弱精症患者的不育原因提供客观参考依据,并有助于对生育力进行评价,有助于临床制定治疗方案。

目前关于精索静脉的超声分级标准尚未统一,通常以精索静脉最大内径结合诊断[12]。但在实际运用中发现,Valsalva实验时个体间差异较大,由于这种个体身体素质差异以及其他因素影响精索静脉血流情况,容易造成误诊。有研究[13]显示VC组与对照组间精索静脉最大流速V/最大内径D比值间差异有统计学意义,说明V/D也可以作为诊断VC的一项重要指标,而不应只限于精索静脉内径的D值、精索静脉返流情况、Valsava试验等。本研究尚未能显示睾丸体积大小与精子质量之间的具体统计学差异,还有待进一步的研究。

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Exploring the relation between related indexes of testis and supersonic inspection of varicocele in patients with asthenozoospermia

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Abstract To explore the relation between related indexes of testis(testicular volume,semen analysis) and supersonic inspection of varicocele in patients with asthenozoospermia. To povide positive basis for the cause of infertility. 129 asthenozoospermia patients(113 cases with VC) and 35 healthy people were inspected by ultrasound,comprising of testicular,parastata,the left spermatic vein maximum daimeter and the time of backflow. The varicoceles were divided into SVC group and VC group including of (VC1,VC2 and VC3). It was compared that the difference of the testis volume and semen analysis between the groups and each other of them. Compared with the normal control group,the left testicular mean volume of VC group was smaller obviously($P<0.01$). Compared between each other in VC groups,the mean volume of left testis was smaller obviously than right ($P<0.05$), the mean volume of testis of VC2 and VC3 group was smaller obviously than the normal control group ($P<0.05$), the mean volume of right testis of VC3 was smaller obviously than the SVC group ($P<0.05$). Compared with the normal control group,the semen analysis of VC group was descending obviously($P<0.01$),and the differences between each other in VC groups were obvious.

Key words asthenozoospermia; varicocele; testis volume; semen; ultrasound

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by combined use of PCR and direct sequencing. ***Results*** The prevalence of BRCA1 mutations in 130 TNBC cases was 17.7%(23/130). There was no statistically significant difference in prevalence of BRCA1 mutations between Han(20.5%,17/83) and minority cases(12.8%,6/47) ($\chi^2=1.856$,$P=0.869$). There had been 23 cases of BRCA1 mutations with 19 loci in 130 cases of TNBC patients, 8 of which were new loci. 4 BRCA1 gene mutation "hot spots" were found. In addition, 9 cases of pathogenic mutations(6.9%, 9/130),including 5 cases of nonsense mutations, 4 cases of frameshift mutations. The prevalence of BRCA1 mutations in 46 early onset breast cancer cases was 28.3%(13/46), which was higher than that in the late onset group (11.9%,10/84),and the difference was statistically significant($\chi^2=5.460$,$P<0.05$). Compared with patients without BRCA1 mutations, who with it had earlier age of onset, higher rate of axillary lymph node metastasis and later of TNM stage,the differences were statistically significant($P<0.05$). ***Conclusion*** The prevalence of BRCA1 mutations in patients with TNBC is higher in multi-ethnic region of Xinjiang. Differences exist in clinical and pathological features between patients with BRCA1 gene mutation and without it.

Key words TNBC; BRCA1 genes; mutation; DNA sequence analysis; clinical pathological features