ORIGINAL ARTICLE

Eur. J. Anat. 22 (2): 119-125 (2018)

Variation in the anatomy of the ligamentum arteriosum in a South African sample

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SUMMARY

The ligamentum arteriosum is a remnant of the ductus arteriosus, which connects the aortic arch and the pulmonary trunk during fetal life. Variation in the anatomy of the ligamentum arteriosum, its connections with the aorta and pulmonary trunk and the course of the left recurrent laryngeal nerve relative to the ligamentum arteriosum were investigated. Dissection of the superior mediastinum was performed on 40 cadavers. The anatomy of the ligamentum arteriosum and its relationship to the aortic arch, pulmonary trunk and left recurrent laryngeal nerve were documented. The dimensions of the ligamentum arteriosum were measured with a caliper. Ligamenta arteriosa in which presence of a lumen was suspected were examined histologically.

Variation in the structure and size of the ligamenta arteriosa was found to be common. A 'line' on the luminal surface of the aorta at the attachment site of the ligamentum arteriosum was observed in 26%. A shallow fossa or depression was found on the luminal surface of the pulmonary trunk in all but one individual. The left recurrent laryngeal nerve was situated lateral to the ligamentum arteriosum in 97%. Variation in the anatomy of the ligamentum arteriosum was found to be common, whereas variation in the position of the left recurrent laryngeal nerve was rare. This information is relevant for surgeons to avoid accidental injury to variant structures. Remnants, in the form of 'lines' or depressions, of the anatomical association between the ductus arteriosus and the aorta and pulmonary trunk were present.

Key words: Ligamentum arteriosum – Aortic arch – Pulmonary trunk – Left recurrent laryngeal nerve – Anatomical variation – Ductus arteriosus

INTRODUCTION

The ligamentum arteriosum is a remnant of the ductus arteriosus, a small artery that connects the arch of the aorta and the pulmonary trunk during embryonic and fetal life. The ductus arteriosus directs blood from the pulmonary trunk into the aorta to bypass the pulmonary circulation. Increased oxygen levels in the blood after birth cause the smooth muscle wall of the ductus arteriosus to constrict, closing off this pathway. The ductus arteriosus subsequently degenerates into a fibrous ligamentum arteriosum, which is located between the arch of the aorta and the pulmonary trunk in the superior mediastinum (Abrams, 1958; Wiyono et al., 2008). Occasionally the ductus arteriosus fails to close, resulting in a patent ductus arteriosus (PDA). PDA is diagnosed clinically when the ductus arteriosus is still open in term infants older than three months of age (Borow et al., 1981; Forsey et al., 2009).

Postnatal anatomical changes in the ligamentum arteriosum are also known to occur, and include calcification and bone formation. Calcification of the ligamentum arteriosum has been observed in both children and adults during computed tomography (CT) imaging (Wimpfheimer et al., 1996, cited in Hong et al., 2012).

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Submitted: 30 August, 2017. *Accepted:* 20 December, 2017.

The length and width of the ligamentum arteriosum are known to vary between individuals, while remnants of the embryological connection between the ductus arteriosus and associated arteries may still be seen in the adult. Gambu et al. (2009, unpublished observations) and Schwab et al. (2013, unpublished thesis) described a ridge on the luminal surface of the aorta that corresponded to the position of the ligamentum arteriosum. A dimple-like feature has also been observed on the luminal surface of the pulmonary trunk in an adult cadaver (Bhatnagar et al., 1996). This dimple corresponded to the site of attachment of the ligamentum arteriosum and was considered to be a remnant of the opening of the ductus arteriosus into the pulmonary trunk (Bhatnagar et al., 1996). No additional reports on the presence or prevalence of this dimple have been found.

The ligamentum arteriosum has a close anatomical relationship with the left recurrent laryngeal nerve (LRLN)(Higgins,1927). The LRLN is a branch of the left vagus nerve and arises as the nerve crosses over the aortic arch. The LRLN loops around the aortic arch on the lateral side of the ligamentum arteriosum, after which it passes through the aortopulmonary window and travels upwards in the tracheoesophageal groove in the neck towards the larynx (Higgins, 1927; Lardinois et al., 1999; Nakahira et al., 2001).

Knowledge of variations in the relationship between the ligamentum arteriosum and the left recurrent laryngeal nerve is relevant for surgeons who operate on structures in the neck and mediastinum. Injury to the laryngeal nerves can, for example, result in permanent hoarseness of the voice (Higgins, 1927). In addition, changes in the ligamentum arteriosum such as calcification or the presence of an opening may be observed on radiographs and could create confusion if not correctly identified as a feature of the ligamentum arteriosum. Calcification of the ligamentum arteriosum may be incorrectly diagnosed as a pathological mediastinal calcification, or even cancer (Bisceglia and Donaldson, 1991).

There have been few studies documenting the anatomy of the ligamentum arteriosum and its relationship to other structures, such as the left recurrent laryngeal nerve and the luminal surfaces of the aorta and pulmonary trunk. Studies to date have been undertaken in Europe, the United States, the Middle East and Asia, with no studies, to our knowledge, reported in Africa.

The aim of this study was thus to investigate and document the following: anatomical changes in the ligamentum arteriosum, such as calcification or patency; variations in the dimensions of the ligamentum arteriosum; the presence of any remnants of the association between the ductus arteriosus and the aorta and pulmonary trunk; and finally, any variation in the position of the left recurrent laryngeal nerve relative to the ligamentum arteriosum.

MATERIALS AND METHODS

A cross-sectional study of embalmed cadavers was undertaken during the year 2010 at the University of Cape Town's Faculty of Health Sciences. The lower neck region and the superior mediastinum were dissected and examined for evidence of variation in the ligamentum arteriosum.

The sample comprised 40 individuals, of which 27 were males and 13 were females. Ages ranged from 29 to 96 years.

The cadavers in this study were utilised in the dissection course for medical students. Any cadavers in which the ligamentum arteriosum, aortic arch, pulmonary trunk or the LRLN had been damaged by prior dissection were excluded from this study. Individuals with atherosclerotic plaques obstructing the luminal surface of the aorta or the pulmonary artery were also excluded.

For each individual, the ligamentum arteriosum, aortic arch, pulmonary trunk, left vagus nerve and the left recurrent laryngeal nerve were identified, exposed and cleared of connective tissues by means of standard dissection techniques.

The anatomy of the ligamentum arteriosum and the course of the left recurrent laryngeal nerve was documented by means of photographs and written descriptions. The aortic arch and the pulmonary trunk, with the ligamentum arteriosum connecting them, were excised with scissors and removed from individuals for further examination. These

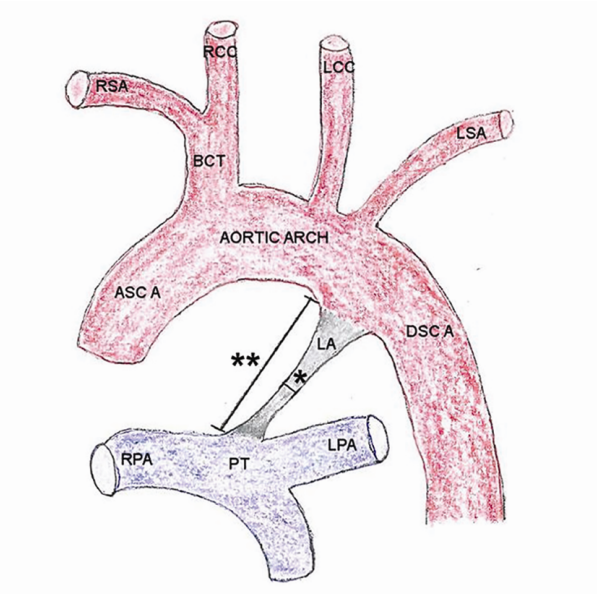

Fig 1. The length (**) of the ligamentum arteriosum (LA) was measured between its attachment points to the aorta and pulmonary trunk (PT) and the width (*) was measured at its midpoint. Abbreviations: ASC A: ascending aorta, BCT: brachiocephalic trunk, RSA: right subclavian artery, RCC: right common carotid, LCC: left common carotid, LSA: left subclavian artery, DSC A: descending aorta, RPA: right pulmonary artery, LPA: left pulmonary artery.

structures were stored in 4% formalin and labelled with a number that corresponded to that of the cadaver from which they were removed.

The dimensions of each ligamentum arteriosum were measured with an electronic digital Vernier caliper (ORIGIN 0-150 mm). The total length of the ligamentum arteriosum between its attachment to the aorta and pulmonary trunk was measured on the ventral side (Fig. 1). The width of each ligamentum arteriosum was measured at its midpoint. The measurements were repeated three times and the average was recorded to reduce intra-observer error. Statistica™ Version 10 was used to determine any correlation between the lengths and widths of the ligamentum arteriosum.

To determine whether the ligamentum arteriosum was obliterated or patent, a piece of fishing line (Speed Spin 100m) 0.60 mm in diameter was gently probed into the ligamentum arteriosum at the luminal aspect of its pulmonary and aortic attachment sites. The ligamentum arteriosum was then incised approximately midway along its length with scissors to assess macroscopically for the presence of a lumen.

The wall of the aortic arch was opened by means of an incision that extended along its ventral aspect to the origin of the left subclavian artery. The luminal surface was exposed and examined for any evidence of thickenings or ridges associated with the ligamentum arteriosum.

The pulmonary trunk was also opened by an incision along its ventral aspect to examine the luminal surface at the site of attachment of the ligamentum arteriosum. Any markings or ridges in the aortic arch or pulmonary trunk were documented and photographed.

Histological examination of two ligamenta arteriosa in which the presence of a lumen was suspected was undertaken. A section of the ligamentum arteriosum was removed from the mid-region using a scalpel with size 10 blade. The samples were processed and embedded in separate wax blocks. Sections measuring 4 µm were cut using a Reichert-Jung Autocut 2040 microtome. The sections were stained with Haemotoxylin and Eosin (H&E) and Elastin von Gieson's (EVG).

The slides were viewed by four observers using a Nikon multiheader light and fluorescent microscope on 4x, 10x and 40x objective magnifications, with eyepiece magnification of 10x.

This study was part of a larger project that was initiated in 2005 and approved by the Ethics Committee on May 18, 2005. An amended ethics approval was obtained on July 2, 2008 to include the current study.

Table 1. Total number of cadavers with sex and anatomical structures examined.

	Total	Male	Female
Ligamentum arteriosum	36	23	13
Length of ligamentum arteriosum	30	17	13
Width of ligamentum arteriosum	31	18	13
Luminal surface of the aortic arch	39	27	12
Luminal surface of pulmonary trunk	33	20	13
Left recurrent laryngeal nerve	30	20	10

RESULTS AND DISCUSSION

As the cadavers had already been dissected by medical students during routine dissection practical sessions, some of the relevant structures had been damaged or removed in some individuals. Table 1 shows the total number of individuals, and their sex, in which the various structures were examined.

Ligamentum Arteriosum

The ligamentum arteriosum was observed passing between the pulmonary trunk and the aortic arch in all of the individuals.

Obliterated ligamenta arteriosa were observed in 26 individuals (72.2%), calcified ligamenta arteriosa were observed in six individuals (16.7%), and in four individuals (11.1%), an opening, which was too small for reliable measurements, was observed in the mid-region (Table 2). In these latter four individuals, however, the ligamentum arteriosum appeared to be closed at both the aortic and pulmonary ends and therefore could not be considered as a patent ductus arteriosus. Histological examination of two of these ligamenta arteriosa revealed that the opening may be an artefact in one individual as no endothelial cells were observed lining the opening. In the second individual however, endothelial cells were observed, suggesting that the opening may be a remnant where the intimal surface of the ductus arteriosus did not unite fully in the middle, thereby leaving a small opening. This description of an opening has previously been documented by Ho and Anderson, 1978. Jager and Wollenman (1942) noted that a microscopic lumen may remain for several months or longer after closure at birth. They observed that the aortic and pulmonary ends of the ductus arteriosus close before the central portion does and thus, the micro-

Table 2. Prevalence of characteristics of the ligamentum arteriosum with respect to sex.

Ligamentum arteriosum	Number of males (%)	Number of females (%)
Obliterated	18 (78.3)	8 (61.5)
Calcified	3 (13.0)	3 (23.1)
Opening in mid-region	2 (8.7)	2 (15.4)

scopic lumen does not appear to be pathological in nature.

There did not appear to be any association between calcification of the ligamentum arteriosum and age, as calcified ligamenta arteriosa were found in individuals who ranged from 37 to 96 years. Calcification has been previously reported in children and adults, although it is suggested that it is not atherosclerotic in aetiology in children, as appears to be the case in older individuals (Bisceglia and Donaldson, 1991; Wimpfheimer et al., 1996, cited in Hong et al., 2012). Hong et al. (2012) found calcification to be more prevalent in children (37.8%) than in adults (11.2%) on multi-section spiral CT. Other reports have shown calcification to be more common in adults, although these studies were done using conventional CT, which has a lower image quality and is therefore less sensitive than multi-section spiral CT (Bisceglia and Donaldson, 1991; Wimpfheimer et al., 1996, cited in Hong et al., 2012).

The prevalence of calcification in this study was lower than the 48% reported by Wimpfheimer et al. (1996, cited in Hong et al., 2012). These authors, however, used CT imaging, which may be more likely to detect calcification than direct observation as is the case in this study.

Calcified ligamenta arteriosa were equally distributed among males and females. Other studies have however shown that calcification is more common in females than in males (Wimpfheimer et al., 1996, cited in Hong et al., 2012). The difference in the findings of this study and other studies may be a reflection of sample size. Wimpfheimer et al. (1996) study comprised 402 individuals, whereas only 36 individuals were examined in this study.

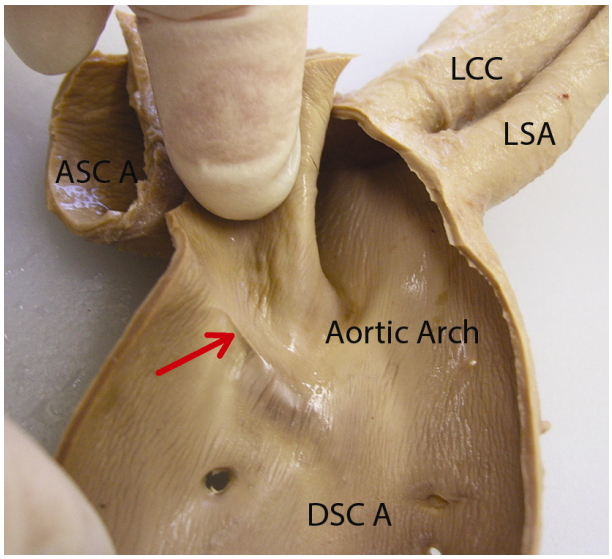

Fig 2. The position of the line (indicated by an arrow) on the luminal surface of the aorta at the site of attachment of the ligamentum arteriosum. Abbreviations: ASC A: ascending aorta, LCC: left common carotid artery, LSA: left subclavian artery, DSC A: descending aorta.

No evidence of bone in the ligamentum arteriosum was found in this study. The lengths of the ligamenta arteriosa ranged from 3.48 mm to 31.28 mm, with a mean length of 14.65 mm (standard deviation 7.33 mm), which is similar to those described by Bhatnagar et al. (1996) for adults (range: 8 - 40 mm, mean 15.47 mm). The range of lengths in infants was recorded as 7.5 - 11 mm, with a mean value of 9.5 mm (Bhatnagar et al., 1996), indicating that variation in the length of the ligamentum arteriosum is normal.

The widths of the ligamenta arteriosa ranged from 1.54 mm to 4.58 mm, with a mean width of 2.86 mm (standard deviation 0.87 mm). These measurements are similar to those recorded by Delmas and Eralp (1953, cited in Bhatnagar et al., 1996), who reported a mean width of 2.94 mm (range: 1.50-5.00 mm). Given that a range in size of the ligamentum arteriosum in individuals has also been reported in the literature and that all the ligamenta arteriosa were obliterated, variation in length and width does not appear to influence closure of the ductus arteriosus.

No significant correlation was found between the lengths and the widths of the ligamentum arteriosum ($p > 0.05$) ($p = 0.177$).

Aortic Ridge

With regards to visible remnants of the relationship between the ductus arteriosus and the aorta, no pronounced ridges on the luminal surface of the aorta, as described by Gambu et al. (2009, unpublished observations) and Schwab et al. (2013, unpublished thesis) were observed, although a slight elevation or 'line' was present in ten individuals (25.6%) (Fig. 2). The 'line' was observed in seven males (26.0%) and three females (25.0%). The 'line' was at the site of attachment of the ligamentum arteriosum in six individuals, and was just distal to this position in four individuals. Table 3 shows the position of the 'line' with respect to the sex of the individuals.

The 'line' found was neither as prominent nor as prevalent as the ridge described by Gambu et al. (2009, unpublished observations) and Schwab et al. (2013, unpublished thesis), who report its presence as 74% and 100% in their respective samples. These differences could be a reflection of sample size and the ages of the individuals examined. For example, the previous studies comprised

Table 3. Position of the aortic 'line' with respect to sex.

Position of the aortic 'line'	Number of males (%)	Number of females (%)
At site of the ligamentum arteriosum	4 (57.1)	2 (66.7)
Distal to site of the ligamentum arteriosum	3 (42.9)	1 (33.3)

large mortuary samples that included infants, children and adults that had not been embalmed, unlike the sample in this study.

The 'line' was predominantly found in younger individuals, with 60% of individuals with the 'line' being below the age of 50 years. Six individuals were under the age of 50 years (33 to 47 years) and three were older than 50 (56 to 60 years), while the age of one individual was not known. This is consistent with the observations of Gambu et al. (2009, unpublished observations), in which the ridge was predominantly found in younger individuals, with a prevalence of 84% in individuals aged 11-25 years, 71% in individuals aged 26-50 years, and 53% in those aged 50 years and older. Schwab et al. (2013, unpublished thesis) observed the ridge in all of the infants and children that they studied. Owing to its high prevalence in neonates and young individuals, these authors suggest that the ridge may be a normal anatomical feature that is present before birth and regresses with age.

Prevalence of the 'line' in this study with respect to sex also differed to that of the ridge (Gambu et al., 2009, unpublished observations). The 'line' was observed with equal prevalence in males and females, whereas Gambu et al. (2009, unpublished observations) found the ridge to be more prevalent in males. Their study, however, consisted of a larger sample of 150 individuals, which could account for this variation.

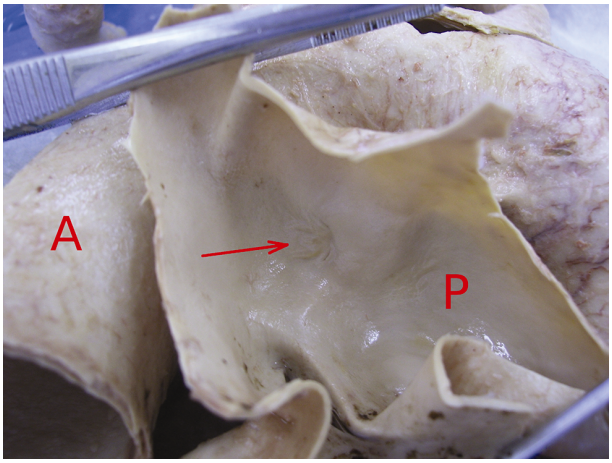

Fig 3A.

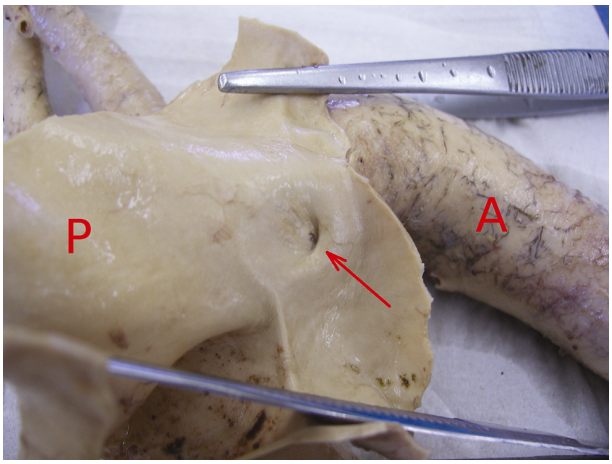

Fig 3B. A small (A) and a large (B) dimple (indicated by arrows) on the pulmonary trunk at the site of insertion of the ligamentum arteriosum. A: aorta, P: pulmonary trunk.

Dimple on luminal surface of pulmonary trunk

The site of attachment of the ligamentum arteriosum on the luminal surface of the pulmonary trunk was marked by an indentation or dimple (Fig. 3), which has previously been described by Bhatnagar et al. (1996). The dimple was present in 32 of the 33 (97%) individuals in this study and absent in only one male, who was 59 years old. It is possible that the dimple may be a remnant of the ostium by which the ductus arteriosus opened into the pulmonary trunk during fetal life. A dimple may be formed when the ductus arteriosus constricts and the openings into the aorta and pulmonary trunk are then closed.

The dimples varied in size and in depth, ranging from 0.1 mm (small) to approximately one centimetre in length (large). The size of the pulmonary dimple did not appear to be associated with the size of the ligamentum arteriosum. There were some individuals in which a large dimple was present with a small ligamentum arteriosum, while in others, a small dimple was present with a wide ligamentum arteriosum. These observations suggest that the dimensions of the ligamentum arteriosum do not determine or influence the size of the dimple.

Left recurrent laryngeal nerve

The left recurrent laryngeal nerve was lateral to the ligamentum arteriosum in 29 of 30 individuals, which is the pattern typically described in the anatomical literature (Fig. 4A). In one individual only, the LRLN passed medial to the ligamentum arteriosum (Fig. 4B).

The LRLN is associated with the sixth aortic arch during embryological development (Khaki et al., 2007). The LRLN follows a course that is inferior to the sixth aortic arch, resulting a position lateral to the ligamentum arteriosum (Khaki et al., 2007). The medial position of the LRLN is a rare variation which may be a result of the nerve passing inferior to the fifth arch instead of the sixth arch. Khaki et al. (2007) observed this rare medial position in a male cadaver as described in a case report.

It has been suggested by Leonard et al. (1983, cited in Khaki at al., 2007) that the mechanical support provided by the LRLN to the ductus arteriosus during embryological development may assist in closure of the ductus arteriosus by inducing the formation of the muscular tunica media. Migration of smooth muscle cells from the tunica media is essential for obliteration of the ductus arteriosus (Imamura et al., 2000). Thus, it might be expected that in individuals in which the LRLN is medial to

Fig 4A. Lateral position (A) and medial position (B) of the left recurrent laryngeal nerve. Key: Light blue: aortic arch, black: brachiocephalic trunk, white: left common carotid artery, dark blue: left subclavian artery, orange: left vagus nerve, pink: left recurrent laryngeal nerve, yellow: ligamentum arteriosum.

Fig 4B.

the ductus arteriosus, the ductus arteriosus would remain open in the absence of the support offered by the nerve. The ligamentum arteriosum was, however, obliterated in the single individual in which the LRLN passed medially to the ligamentum arteriosum in this study.

Although variation is present at very low frequency, knowledge that the LRLN may be situated on the medial side of the ligamentum arteriosum is clinically important, as the nerve may be damaged during surgery on the aorta or ligamentum arteriosum (Khaki et al., 2007).

Limitations and recommendations for future studies

A relatively small sample of adult cadavers that had been previously dissected by medical students was available for the study. In addition, these cadavers had been fixed in formalin, which is known to cause tissue shrinkage (Jonmarker et al., 2006). This may have affected certain parameters such as the dimensions of the ligamentum arteriosum. Examination of non-embalmed tissues would provide useful comparative material.

Further studies on a larger and more wide-ranging population, particularly with respect to age, would enhance current knowledge of variations in these structures. Additional research is necessary to investigate whether calcification of the ligamentum arteriosum is associated with calcification of other structures, such as the valves of the heart or the aorta.

Conclusion

Variations in the anatomy of the ligamentum arteriosum and the left recurrent laryngeal nerve exist in South African samples. Knowledge of these variations is of relevance to surgeons who operate on the mediastinum and thorax. Changes in the ligamentum arteriosum such as calcification and the presence of an opening may be observed on radiographs and could create confusion if not identified as a feature of the ligamentum arteriosum. The presence of an opening in the mid-region of the ligamentum arteriosum does not necessarily mean it is patent as aortic and pulmonary ends may be closed. Clinicians also need to be aware that variations in the dimensions of the ligamentum arteriosum are not uncommon.

ACKNOWLEDGEMENTS

The body donors and their families for their generous gift. National Research Foundation and the University of Cape Town for funding the research.

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