Central core of the cerebrum

Laboratory investigation

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Object. The purpose of this study was to understand 3D relationships of white matter fibers and subcortical areas of gray matter in the central core.

Methods. The lateral and medial aspects of 4 cerebral hemispheres were dissected, applying the fiber dissection technique under the microscope.

Results. The central core between the insula and midline includes the extreme, external, and internal capsules; claustrum; putamen; globus pallidus; caudate nucleus; amygdala; diencephalon; substantia innominata; fornix; anterior commissure; mammillothalamic tract; fasciculus retroflexus; thalamic peduncles, including optic and auditory radiations; ansa peduncularis; thalamic fasciculus; and lenticular fasciculus. It is attached to the remainder of the cerebral hemisphere by the cerebral isthmus, which is composed of white matter fibers located between the dorsolateral margin of the caudate nucleus and the full circumference of the circular sulcus of insula. The rostral fibers of the corpus callosum are included in the frontal portion of the cerebral isthmus.

Conclusions. It is very useful for neurosurgeons to facilitate the understanding of spatial relationships and pertinent surgical approaches in and around the central core with a highly complex anatomy by using fiber dissection. (DOI: 10.3171/2010.9.JNS10530)

KEY WORDS • central core • fiber dissection • neuroanatomy • cadaver dissection

HE deep central region of the cerebral hemispheres is composed of several subcortical areas of gray matter and highly complex white matter fibers. This region is referred to as the central core.¹⁶ From the standpoint of function, it has been known to play an important role in motor and sensory functions, emotion, endocrine integration, and cognition, despite its relatively small size. Most studies about the neuroanatomical organization in and around the central core have been based on histological, anatomical, and radiological studies that require the reader to reconstruct this region from many consecutive 2D images.^{7,13,16,18} We have seldom seen 3D pictures showing the spatial relationships of white matter fibers and deep central areas of gray matter in and around the central core. Recently, diffusion tensor tractography has been found to be useful in investigating white matter fibers of the brain, although it could not demonstrate fiber tracts exactly due to some limitations.⁵ On the other hand, doing fiber dissections has some advantages, through practical experience, in facilitating 3D understanding of both white and gray matter simultaneously and in investigating some fibers that are not delineated by diffusion tensor tractography. Therefore, we attempt to discuss the neuroanatomy of the central core by using fiber dissections.

Methods

Four human cerebral hemispheres were dissected from the lateral, medial, and inferior aspects in and around the central core under the microscope by using fiber dissection techniques, which have been described very well in several previous reports.^{9,10,14,15,19} Three coronal cuts of the dissected cerebral hemisphere at the anterior, middle, and posterior positions of the circular sulcus of the insula were made to identify the relationships between the ventricle or caudate nucleus and the circular sulcus of the insula.

Results

Lateral Dissections of the Central Core

Frontal, parietal, and temporal operculi around the sylvian fissure of the left cerebral hemisphere were dissected. The dorsal portions of the insula and its circular sulcus were surrounded by the superior longitudinal fasciculus, which was located deep in relation to the frontoparietotemporal operculi. The frontal and temporal ends of the circular sulcus of the insula approached the limen insulae and were not connected with each other (Fig. 1A). The extreme capsule, claustrum, and external



Fig. 1. Consecutive dissections of the central core accomplished from the lateral aspect of the left cerebral hemisphere. Curved red and blue lines represent the superior and inferior circular sulci of the insula, respectively. The upper and lower cerebral isthmuses are located deep in relation to the superior and inferior circular sulci of the insula, respectively. A: The short and long arcuate fibers and frontal, parietal, and temporal opercular cortices have been dissected. The superior longitudinal fasciculus surrounding the insula and its circular sulcus dorsally is seen deep in relation to the frontoparietotemporal opercular cortices. The frontal and temporal ends of the circular sulcus of the insula approach the limen insulae and are not connected with each other. B: The ventral extreme capsule, claustrum, and dorsal external capsule are seen deep to the removed insular C: The superior longitudinal fasciculus, extreme capsule, claustrum, external capsule, inferior frontooccipital fasciculus, cortex. uncinate fasciculus, and anterior commissure have been dissected. The anterior commissure passes just inferior to the middle base of the putamen, and its lateral extensions have been resected. Radiating fibers around the putamen (corona radiata) are seen, and the Meyer loop with curved striations, constituting the anterior bundle of the optic radiation, is seen in the temporal lobe. D: The putamen and the thalamic peduncles have been removed, and the wall of the lateral ventricle is exposed. The tapetum, caudate nucleus, amygdala, stria terminalis, globus pallidus, thalamus, and internal capsule are seen. The internal capsule separates the lenticular nucleus from the caudate nucleus and thalamus. The stria terminalis proceeds in the groove between the thalamus and caudate nucleus from the amygdala to the septal area. E: The globus pallidus has been removed and the resected anterior commissure is reflected. The ansa peduncularis passes through the substantia innominata to the septal area and curves outside the internal capsule. It is positioned inferior to the anterior commissure and the globus pallidus, and superior to the anterior perforated substance. The ventral portion of the head of the caudate nucleus is interspersed with the substantia innominata.

capsule were seen deep in relation to the insular cortex (Fig. 1B).

The superior longitudinal fasciculus, extreme capsule, claustrum, external capsule, inferior frontooccipital fasciculus, uncinate fasciculus, and anterior commissure were dissected. The anterior commissure was inferior to the base of putamen, and its lateral extension was resected to expose a small hidden part of the putamen and optic radiations. The corona radiata, including the thalamic peduncles, was observed around the putamen. The Meyer loop with curved striations, an anterior bundle of the optic radiation, was located near the tip of the temporal horn (Fig. 1C).

The putamen and thalamic peduncles were dissected to expose the tapetum, caudate nucleus, amygdala, stria terminalis, globus pallidus, thalamus, and internal capsule. The internal capsule separated the lenticular nucleus from the caudate nucleus and thalamus. The stria terminalis, which arises from the amygdala, proceeded in the groove between the thalamus and the caudate nucleus (Fig. 1D). The globus pallidus was removed. The ansa peduncularis was seen, passing through the substantia innominata to the septal area, curving outside the internal capsule. It was located inferior to the anterior commissure and globus pallidus, and superior to the anterior perforated substance. The head of the caudate nucleus was interspersed with substantia innominata (Fig. 1E).

Medial Dissections of the Central Core

The corpus callosum and septum pellucidum were dissected and the medial temporal lobe, including the hippocampus and parahippocampal gyrus, was removed to open the temporal horn and atrium of the lateral ventricle. The caudate nucleus, including its head and body in the lateral ventricle, was seen through the window made by the resected septum pellucidum. The taenia, a reflection of the ependyma, continued to the tela choroidea, forming the roof of the third ventricle. The tela choroidea, together with the choroid plexus, invaginated laterally from the velum interpositum into the lateral ventricle through the choroidal fissure. The stria medullaris appeared as a

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small transverse bundle running from the interventricular foramen to the habenula and separated the dorsal from the medial diencephalic surface. The hypothalamic sulcus, a shallow transverse groove from the interventricular foramen to the aqueduct of Sylvius on the third ventricular surface, separated the dorsal thalamus from the ventral hypothalamus (Fig. 2A).

The corpus callosum, tela with choroid plexus, and hippocampal commissure were removed to expose the medial aspect of the central core. The caudate nucleus curved down along the laterosuperior wall of the lateral ventricle. The medial diencephalic surface was surrounded by the stria medullaris, foramen of Monro, anterior commissure, lamina terminalis, optic chiasm, habenular commissure, pineal body, posterior commissure, aqueduct, midbrain tegmentum, mammillary body, and infundibulum. The distance between the anterior and posterior commissure was an average of 25 mm (Fig. 2B).

In the superior view, the dorsal diencephalic surface was divided by the fornix into the lateral region (floor of the lateral ventricle), which was covered by the ependyma, and the medial region (roof of the third ventricle), which was covered by the tela choroidea. In the lateral region, the stria terminalis connecting the septal area to the amygdala runs in the groove between the thalamus and caudate nucleus (Fig. 2C). In the posterior view, continuations of the caudate nucleus, stria terminalis, and fornix curved down toward the superior wall of the temporal horn. The fornix continued to its crus and fimbria, forming the hippocampal commissure, which made up the medial wall of the lateral ventricle. Also, the caudate nucleus continued to its tail, which was continuous with the amygdala. The pulvinar, habenula, and pineal body were identified. The superior and inferior colliculi extended to the lateral and medial geniculate bodies, respectively (Fig. 2D).

The ependymal layer of the lateral and third ventricles was removed. Fine fiber striations coursing in a transverse direction were observed in the medial diencephalic surface, and the tapetum surrounded the lateral ventricular wall. The anterior thalamic peduncle, passing through the lateral region to the head of the caudate nucleus, was seen near the anterior thalamic pole. The precommissural fornix located anterior to the anterior commissure proceeded to the septal region. The striations seen superior to the hypothalamic sulcus looked more prominent than those observed below it, and they ran from the dorsal parts of the hypothalamus to the ventromedial parts of the thalamus, to the tegmentum of the midbrain. The striations observed inferior to the hypothalamic sulcus appeared to be loose, and they ran from the ventral parts of the hypothalamus to the tegmentum of the midbrain. Hypothalamic nuclear groups with gray coloring did not show any clear demarcation (Fig. 2E).

Lateral to the hypothalamic nuclei, the postcommissural fornix and mammillothalamic tract were dissected. These fiber tracts were the most prominent structures in this area. Just superior to the anterior commissure, the fornix was divided into the slender precommissural and thicker postcommissural tracts. The postcommissural fornix continued to the mammillary body and provided several connections to the anterior thalamus, hypothala-

b the ventromedial parts insula, respectively. The cert of white matter fibers locate of the insula and the dorso nucleus. The anterior part of

mus, and habenula via the stria medullaris. The mammillothalamic tract connected the mammillary body to the anterior thalamus (Fig. 2F). In the region located lateral to the postcommissural fornix (superior to the optic tract and inferior to the anterior commissure), the transverse striations located outside the internal capsule with longitudinal striations were seen. These striations continued to the ansa peduncularis, which was passing through the substantia innominata observed in the lateral dissection of the cerebral hemisphere (Fig. 2G).

The thalamic nuclei and mammillothalamic tract were removed. The thalamic fasciculus with longitudinal striations ran toward the region lateral to the red nucleus. The fasciculus retroflexus, connecting the habenula to the interpeduncular nucleus, was dissected just medial to the red nucleus (Fig. 2H). The zona incerta, a thin gray matter sheet lying medial to the internal capsule, appeared as a bright area of gray matter after the thalamic fasciculus was removed (Fig. 2I). Below the zona incerta, the lenticular fasciculus with oblique striations passing through the internal capsule from the globus pallidus reached the prerubral area (region anterolateral to the red nucleus) to meet the ansa lenticularis, which was a part of the ansa peduncularis (Fig. 2J). In the region posteroinferior to the lenticular fasciculus, an ovoid subthalamic nucleus with a biconvex shape lay just medial to the internal capsule and superior to the substantia nigra (Fig. 2K).

Identification of the Cerebral Isthmus

The frontotemporal base of the left cerebral hemisphere was dissected to see the frontotemporal ends of the caudate nucleus and circular sulcus of the insula. The ventral portion of the head of the caudate nucleus was surrounded by the rostral fibers of the corpus callosum and was continuous with the substantia innominata. The rostral fibers of the corpus callosum reached the limen insulae at least, and were located just medial to the uncinate fasciculus and inferior frontooccipital fasciculus. The tail of the caudate nucleus was continuous with the amygdala, which was covered by the uncinate fasciculus. The dorsolateral margin of the caudate nucleus could be the inner opposite line to the outer circular sulcus of the insula as the borders of the central core (Fig. 3A).

The cerebral isthmus was identified on 3 coronal sections at the anterior (Fig. 3B), middle (Fig. 3C), and posterior (Fig. 3D) positions of the circular sulcus of the insula, respectively. The cerebral isthmus was composed of white matter fibers located between the circular sulcus of the insula and the dorsolateral margin of the caudate nucleus. The anterior part of the upper cerebral isthmus separated the superior circular sulcus of the insula from the frontal horn of the lateral ventricle. The lower cerebral isthmus was positioned between the inferior circular sulcus of the insula and the temporal horn of the lateral ventricle. The posterior parts of the upper and lower cerebral isthmus separated the superior and inferior circular sulci of the insula and the atrium of the lateral ventricle. All projection fibers and the extreme capsule were in the cerebral isthmus. In addition, frontal and temporal portions of the cerebral isthmus included rostral fibers of the corpus callosum, frontal extensions of the uncinate fas-



Fig. 2. Consecutive dissections of the central core accomplished from the medial aspect of the right cerebral hemisphere. A: The corpus callosum has been dissected, and the septum pellucidum and medial temporal lobe have been removed. The head and body of the caudate nucleus in the lateral ventricle are seen. The tela choroidea together with the choroid plexus invaginates laterally from the velum interpositum into the lateral ventricle through the choroidal fissure. The stria medullaris connecting the septal region to the habenula separates the dorsal diencephalic surface from the medial diencephalic surface. The medial diencephalic surface is divided by the hypothalamic sulcus (dotted line) into the thalamus above and the hypothalamus below and lies between the foramen of Monro and the aqueduct; it is surrounded by the stria medullaris, anterior commissure, lamina terminalis, habenular commissure, pineal body, posterior commissure, aqueduct, midbrain tegmentum, and mammillary body. B: The corpus callosum, tela and choroid plexus, and the hippocampal commissure have been removed to expose the medial view of the central core, including the caudate nucleus, fornix, and diencephalon. C: Superior view of the central core showing the dorsal diencephalic surface divided by the fornix into the lateral region (floor of the lateral ventricle) and the medial region (roof of the third ventricle). In the lateral region, the stria terminalis runs in the groove between the thalamus and caudate nucleus. D: Posterior view of the central core showing the continuations of the stria terminalis, caudate nucleus, and fornix curving down toward the superior wall of the temporal horn. The fornix continues to its crus, and the fimbria and tail of the caudate nucleus approach the amygdala. The hippocampal commissure, which makes up the medial wall of the lateral ventricle, has been removed. The pulvinar, habenula, pineal body, and medial and lateral geniculate bodies are seen medial to the fornix. The superior and inferior colliculi extend to the lateral and medial geniculate bodies, respectively, each through its brachium. E: The ependymal layer of the lateral and third ventricles has been removed. Fine fiber striations are observed in the medial diencephalic surface, and the lateral wall of the lateral ventricle is surrounded by the tapetum. The anterior thalamic peduncle seen at the anterior thalamic pole passes through the lateral region to the head of the caudate nucleus. The precommissural fornix located anterior to the anterior commissure proceeds to the septal region. Hypothalamic nuclear groups with gray coloring have no clear demarcation. F: Lateral to the hypothalamic nuclei, the postcommissural fornix and mammillothalamic tract have been dissected. Just superior to the anterior commissure, the fornix is divided into the slender precommissural and thicker postcommissural tracts. The latter continues to the mammillary body after forming the foramen of Monro. The mammillothalamic tract connects the mammillary body to the anterior thalamus. G: In the region located lateral to the postcommissural fornix, superior to the optic tract, and inferior to the anterior commissure, the transverse striations are located outside the internal capsule, with longitudinal striations, and continue to the ansa peduncularis. H: The thalamic nuclei and mammillothalamic tract have been removed. The thalamic fasciculus, with longitudinal striations, runs toward the region lateral to the red nucleus. The fasciculus retroflexus, dissected just medial to the red nucleus, connects the habenula to the interpeduncular nucleus. I: The thalamic fasciculus has been removed. The zona incerta, a thin gray matter sheet located medial to the internal capsule, appears as a bright area of gray matter. J: The zona incerta has been removed. The lenticular fasciculus, with oblique striations, passing through the internal capsule from the globus pallidus, reaches the prerubral area to meet the ansa lenticularis. K: Posteroinferior to the lenticular fasciculus, an ovoid subthalamic nucleus with a biconvex shape lies medial to the internal capsule and superior to the substantia nigra.

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Fig. 3. Red and blue double-arrow lines indicate the upper and lower cerebral isthmus, respectively, in all panels. A: The rostral portion of the corpus callosum, frontal operculum, insula, and temporal lobe of the left cerebral hemisphere have been dissected extensively to show the relationships between the dorsolateral margin of the caudate nucleus and the circular sulcus of the insula. Curved red and blue lines represent the superior and inferior circular sulci, respectively. The curved black line and the area shaded with gray indicate the dorsal margin of the caudate nucleus and the resected tail of the caudate nucleus, respectively. The dorsolateral margin of the caudate nucleus is the inner line opposite to the outer circular sulcus of the insula at the borders of the central core. The ventral portions of the head of the caudate nucleus are surrounded by rostral fibers of the corpus callosum, extending to the limen insulae at least, and are continuous with the substantia innominata. The tail of the caudate nucleus is continuous with the amygdala, which is covered by the uncinate fasciculus. Three coronal sections of the left cerebral hemisphere at the anterior (B), middle (C), and posterior (D) positions of the circular sulcus of the insula have been made. The temporal lobe has been dissected to open the temporal horn. The cerebral isthmus consists of white matter fibers located between the circular sulcus of the insula and the dorsolateral margin of the caudate nucleus. B: The anterior part of the upper cerebral isthmus separates the superior circular sulcus of the insula and the frontal horn of the lateral ventricle. C: The upper and lower cerebral isthmus are shown. The latter, referred to as the temporal stem, is positioned between the inferior circular sulcus of the insula and the temporal horn. D: The posterior part of the upper and lower cerebral isthmus separates the superior and inferior circular sulci of the insula from the atrium of the lateral ventricle.

ciculus, frontal extensions of the inferior frontooccipital fasciculus, and temporal extensions of the uncinate fasciculus, and temporal extensions of the inferior frontooccipital fasciculus, anterior commissure, optic radiations, and auditory radiations.

Discussion

The central core, between the insula and the midline of the cerebral hemisphere, is attached to the remainder of the hemisphere by the cerebral isthmus, which is located deep in relation to the circular sulcus of the insula. It includes the internal, external, and extreme capsules; claustrum; caudate and lentiform nuclei (putamen and globus pallidus); thalamus; and fornix.¹⁶ The central core is an integral area that contains several interrelated structures that perform the mandatory neural functions such as motor, sensory, visual, auditory, autonomic, endocrine, and cognitive functions in spite of its small size. Also, the pathological conditions occurring in this region can spread or compress important adjacent structures easily because of its central position and compact relations. However, due to the central position of the intracranial space and complete encasement in neural tissue, spatial understanding of the central core is not simple, although the anatomy of and relevant surgical approaches to the central core have often been described with schematic drawings and illustrations.^{6,16} Also, surgery of this area has remained limited and challenging for most neurosurgeons. In this regard, we think that fiber dissections have been useful to reconstruct the internal structures of the central core three dimensionally.

In this study, the cerebral isthmus, located between the dorsolateral margin of the caudate nucleus and the circular sulcus of the insula, was the area of white mat-

ter connecting the central core to the remaining cerebral hemisphere, and the lower cerebral isthmus was similar to the temporal stem. It was also noted that the cerebral isthmus was the pathway of all projection fibers and the extreme capsule, and that the frontal portion of the cerebral isthmus included rostral fibers of the corpus callosum, frontal extensions of the uncinate fasciculus, and frontal extensions of the inferior frontooccipital fasciculus. Therefore, it is considered that the dorsolateral margin of the caudate nucleus may be more apparent than the lateral wall of the lateral ventricle to define the cerebral isthmus in detail. Also, we think that the lower cerebral isthmus may be a more appropriate term than the temporal stem, because the term "stem" has been used only in the temporal lobe regionally, and the temporal stem also has some anatomical ambiguity caused by slightly different definitions as well.^{8,14,20,21} Except for transcortical and transcallosal approaches to reach the central core, only the anterior part of the lower cerebral isthmus or anterior temporal stem has been used as a surgical trajectory in the transsylvian approach, even though the anterior part of the upper cerebral isthmus carries less risk than the other parts of the cerebral isthmus.16,22

There are many useful radiological and histological images and schematic drawings, but still these may not be sufficient to understand a highly complex region like the central core three dimensionally. Of several methods used to investigate internal structures of the brain, the fiber dissection technique has shown usefulness in achieving practical experience, resulting in better understanding of the perplexing structures through the consecutive dissection process.^{3,4,15,17,19} Recently, diffusion tensor tractography has also shown excellent images of white matter fiber tracts intermingled inside the brain.^{5,8,14,20} Compared with histological sections, radiological images, and artistic or schematic drawings offered by the majority of

existing texts, we think that fiber dissections and tractography have unique advantages in providing 3D depictions of white matter anatomy especially, although these techniques also have some limitations.^{5,15} However, we have never seen 3D pictures or images taken from fiber dissections or diffusion tensor tractography in the central core, although the lateral aspect of the cerebral hemisphere, including the central core, has been discussed in several previous reports.^{5,15,17,19} We divided the medial aspect of the central core into 3 parts for convenient discussion.

Medial View

The pre- and postcommissural fornices, anterior commissure, stria medullaris, habenular commissure, posterior commissure, indistinct periventricular fibers, amorphous hypothalamic nuclei, ansa peduncularis, mammillothalamic tract demonstrated in 1827,¹¹ thalamic fasciculus, zona incerta, lenticular fasciculus, subthalamic nucleus, and fasciculus retroflexus were identified. Many fine fibers were observed under the microscope, but not all of them could be followed because of their looseness and small size. The periventricular fiber system includes the dorsal longitudinal fasciculus, thalamo-hypothalamic fibers, medial forebrain bundle, mammillo-tegmental fiber, and mammillary peduncle.^{6,13} The supraopticohypophysial and tuberohypophysial tracts also appeared indistinct. The stria medullaris connecting the septal region to the habenula receives fibers from the amygdala; the anterior perforated substance; the olfactory area via the stria terminalis; the hippocampus via the fornix; the hypothalamus; and the midbrain tectum. The anterior commissure was found to be wrapped in a glial tunnel around the midline. The postcommissural fornix continues to the mammillary body and gives several connections to anterior thalamus, hypothalamus, and habenula via the stria medullaris, and to the tegmentum of the midbrain via fine bundles in the wall of the third ventricle.

We could not find all the connections accurately. The ansa peduncularis is composed of 3 different fibers. First, the ventral amygdalofugal fiber, which originates from the basolateral nucleus of the amygdala and the pyriform cortex, and proceeds to the hypothalamus and brainstem. Second, the inferior thalamic peduncle (extracapsular thalamic peduncle), which receives contributions from the amygdala, anterior temporal cortex, and substantia innominata, turns sharply outside the internal capsule to reach the hypothalamus and medial thalamus. Third, the ansa lenticularis, which arises from the globus pallidus, turns outside the internal capsule to meet the lenticular fasciculus in the Forel field H₃ (prerubral area).¹⁵ The fibers and nuclei of the thalamus could not be dissected separately because of highly compact intermingling. The fasciculus retroflexus (Meynert bundle), or habenulointerpeduncular tract, is the largest habenular outflow of the limbic system, and was described in 1872.¹² In the region posterolateral to the red nucleus, there were unidentifiable thick fibers that may have included the central tegmental fasciculus, reticular formation of the midbrain, brachium of the inferior colliculus, and lemniscus fibers.^{6,13} The zona incerta is continuous with the reticular nuclei group of the thalamus.¹ Below that, the longitudinal striations

seen in the region lateral to the red nucleus are considered to be the intracapsular pallidofugal fibers that include pallidonigral and pallidotegmental fibers.¹³

Superior View

The caudate nucleus, small gray matter islands of the septal area, stria terminalis, fornix, and thalamus were identified. The anterior thalamus in the dorsal diencephalic surface has the prominence on the anterior thalamic pole, which is the region posterolateral to the foramen of Monro. The stria terminalis arises from the corticomedial nucleus of the amygdala and gives off several contributions to the hypothalamus and stria medullaris.^{6,13}

Posterior View

The habenula, pineal body, pulvinar of the thalamus, continuations of the fornix, stria terminalis, and caudate nucleus, and the medial and lateral geniculate bodies were identified. The pretectal area, which receives contributions from the occipital cortex and optic tract through the superior colliculus, constitutes the extrageniculate visual pathway.^{6,13}

Regarding the lessons learned from the fiber dissections of the central core, it is essential to compare them with knowledge taken from existing cross-sectional histological and radiological images, and to maintain the patency of fiber striations during dissections to avoid inadvertent damage.^{1,2,6,7}

Conclusions

The central core, which has a highly complex anatomy, can be better understood three dimensionally in the way the fiber dissections appear, together with the existing cross-sectional images.

Disclosure

The authors declare that they do not have any financial supports or relationships that may pose a conflict of interest.

Author contributions to the study and manuscript preparation include the following. Conception and design: all authors. Acquisition of data: Choi. Analysis and interpretation of data: Choi, Yee, Lee. Drafting the article: Choi, Han, Lee. Critically revising the article: Yee, Lee. Reviewed final version of the manuscript and approved it for submission: all authors.

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