INTRODUCTION

When conventional computed tomography (CT) had been the main imaging technique in head and neck evaluation, an additional contrast injection was necessitated because the contrast media washed out during a long scanning time of 4 to 5 minutes (1). Such multiphasic contrast injection allowed an optimal conspicuity of images. As there are multiple vascular structures and lymph nodes in the head and neck space, large vessels with washed-out contrast media within its may interfere with identifying the enhancing lymph node or other solid tissues on the contrast-enhanced head and neck CT.

With the development of multidetector CT (MDCT), the acquisition time became short after contrast media administration, and the risk of motion artifacts resulting from swallowing, respiration, and patient motion decreased (2, 3). Despite these advantages, the short acquisition time on MDCT can engender a risk of lower conspicuity in the images. Contrast with helical...
CT, the immediate scan after the contrast injection on MDCT hinders the goal of acquiring the optimal enhancement of the solid organ. Therefore, it is important to use an optimized scan delay time for the conspicuity of the enhancing tissues. If the scan delay time is long, tissue enhancement increases, yet, vessel evaluation will be limited due to the washout of the contrast in the vessels. The short delay time that allows for the sufficient vessel enhancement can limit the sufficient penetration of the contrast media into the normal or pathologic tissue.

Great effort has been made to acquire optimal images of both tissue and vessel enhancement on the head and neck CT by modulation of technical factors involved in the administration of contrast media, injection rate, scan delay time, and the use of a saline flush (4, 5). However, these studies have not yet focused on the effects of the number of injections on the tissue contrast. Although we could find several articles on multiphasic injections for MDCT, these studies have focused on the cardiovascular imaging of CT angiography (6-9). It was claimed that the multiphasic injection itself was effective for uniform arterial enhancement (8), and it has been reported that biphasic injection had fewer artifacts caused by contrast media in the superior vena cava than in the monophasic injection (6).

Thus, the hypothesis of this study is that if contrast media is injected biphasically with an early and late phase, the attenuation of tissue and vessel will be well maintained. Based on this, the purpose of this study is to evaluate the optimal injection protocol and scan delay time in a CT of the head and neck.

**MATERIALS AND METHODS**

The study population for this prospective study consisted of all consecutive patients who underwent MDCT of the head and neck from January 2007 to June 2007. The study was approved by the Institutional Review Board. The majority of the patients were referred for assessment of a palpable neck mass, for staging of a head and neck tumor, for evaluation of cervical lymph nodes, and for assessment of an acute infection of the head and neck area. Patient’s medical records were reviewed, and those with clinically proven arrhythmia or congestive heart failure were excluded from this study, as these conditions could affect the circulation time. Also, patients with severe stenosis of the carotid arteries, patients younger than 18 years (contrast media was administered at 1.5 mL/kg to children and adolescents under 18 years old), and patients that had technical errors in the scanning procedures were excluded.

CT was performed using a 16 channel MDCT scanner (16-slice Brilliance CT scanner, Philips, Cleveland, OH, USA). A CT scan was performed with the following parameters: 120 kV and 250 mAs, 64 × 0.625 mm slice configuration, 0.75 seconds gantry rotation time, 1.014 pitch, 40.56 mm table feed per rotation, 2 mm section thickness, 5 mm reconstruction slice width, and 0 reconstruction interval. The scanning range covered the area from the skull base to the aortic arch in the cephalocaudal direction using axial slices. Using a power injector (Stellant, Medrad, Indianola, PA, USA), non-ionic contrast medium (Omnipaque, iohexol 300 mg I/mL; Nycomed, Princeton, NJ, USA) was injected through the right antecubital vein.

Two steps were designed in this study. In the first step, four different contrast injection protocols were used to evaluate the effect of biphasic injections on vessel and tissue attenuation. In the second step, we assessed how biphasically injected contrast media affect the contrast volume.

**First Step**

The use of four different contrast injection protocols was compared. The final study population consisted of 77 patients (27 males, 50 females) who ranged in age from 20 to 77 years (mean age, 49.6 ± 13.6 years). The mean height was 160.9 ± 8.1 cm, the mean weight of the patients was 59.9 ± 8.4 kg, and the mean body mass index (BMI) was 23.1 ± 2.9 kg/m². BMI was calculated as body weight/height² (kg/m²) (Table 1).

Each patient was assigned randomly to one of the four protocol groups: a high rate monophasic injection group (M1), a high rate biphasic injection group (B1), a low rate monophasic injection group (M2), and a low rate biphasic injection with a longer delay time group (B2). A bolus of 100 mL of contrast media was administrated for the two monophasic injection groups (M1 and M2). For the two biphasic injection protocols (B1 and B2), an initial bolus of 50 mL of contrast media was administered, and an additional 50 mL of contrast media was then administered 35 seconds after the initiation of the first bolus injection. A flow rate of 3 mL/sec and 2 mL/sec of contrast media was administered for the two high rate injection groups (M1 and B1) as well as for the two low rate injection groups (M2 and B2).
and B2), respectively. The scan delay time, which was the time between the initiation of the intravenous contrast media bolus and the start of the CT scanning, was 70 seconds, based on published optimal values [published recommended values are between 52-76 seconds (5)]. Scans for the B2 protocol group were acquired only with a 120-second delay time. The protocols for each group are summarized in Table 1 and Fig. 1.

For a quantitative analysis, a neuroradiologist measured the CT numbers for each patient in the bilateral arteries (carotid arteries), veins (internal jugular veins), salivary glands (submandibular glands), muscles (sternocleidomastoid muscles), and lymph nodes, of which the transverse diameter was 0.5-1 cm at the level of C2-3 using a region of interest (ROI) cursor. An ROI cursor was circular. The ROI area was defined as more than 7 mm². An ROI was selected when the cursor was not affected by partial volume averaging or by a beam-hardening artifact. After data acquisition, the mean attenuation value of the artery, vein, salivary gland, muscle, and lymph node were calculated for each patient by averaging the attenuation values of the bilateral side. If a unilateral internal jugular vein was occluded, or too small, the attenuation values of the referred vessel at that scanning level were not measured.

Second Step

The purpose of this step was to assess whether the biphasic injection protocol was useful in reducing the total volume of contrast injection. The protocol groups are summarized in Table 1 and Fig. 1.

Table 1. Patient Characteristics and Summary of Contrast Injection Protocols of Six Different Groups in the First and Second Steps

<table>
<thead>
<tr>
<th>Protocol Group</th>
<th>First Step</th>
<th>Second Step</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M1</td>
<td>B1</td>
</tr>
<tr>
<td>Patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.6 ± 14.7</td>
<td>48.9 ± 12.9</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.3 ± 8.1</td>
<td>161.5 ± 7.6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>58.3 ± 8.9</td>
<td>60.0 ± 6.3</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.8 ± 3.8</td>
<td>23.1 ± 2.4</td>
</tr>
<tr>
<td>CT protocol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast volume (mL)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>No. of boluses</td>
<td>Monophasic</td>
<td>Biphasic</td>
</tr>
<tr>
<td>Injection rate (mL/s)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Start of 2nd bolus (s)</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Delay time (s)</td>
<td>35</td>
<td>35</td>
</tr>
</tbody>
</table>

Note: — M1 = a high rate monophasic injection group, B1 = a high rate biphasic injection group, M2 = a low rate monophasic injection group, B2 = a low rate biphasic injection with a longer delay time group, M3 = a low rate monophasic injection with standard volume group, B3 = a low rate biphasic injection with reduced volume group. BMI = body mass index, f = female, m = male, N = number, No. = number
In the second step, the imaging analysis was processed as in the first step. An unpaired t-test was used to determine the statistical differences in CT numbers of each tissue between the two groups.

RESULTS

First Step

Analysis of variance revealed no significant differences between the four patient groups with respect to age, sex, height, weight, and BMI.

The mean CT numbers of the artery were 189.6 ± 20.8, 204.1 ± 23.3, 223.8 ± 35.2, and 189.8 ± 20.3 for M1, M2, B1, and B2 protocols, respectively. The results, as determined by ANOVA, were statistically significant. As determined by the post test, with the same delay time and injection rate, the attenuation of the artery after biphasic injection (B1) was significantly higher than after monophasic injection (M1).

The mean CT numbers of the vein were 198.5 ± 19.3, 243.2 ± 31.2, 214.8 ± 27.0, and 198.5 ± 18.8 for M1, B1, M2, and B2 protocols, respectively. The results, as determined by ANOVA, were statistically significant. As determined by the post test, regardless of the injection rate, the attenuation of the vein after biphasic injection (B1) was significantly higher than after monophasic injection (M1).

The mean CT numbers of the artery were 198.5 ± 19.3, 243.2 ± 31.2, 243.2 ± 31.2, and 198.5 ± 18.8 for M1, B1, M2, and B2 protocols, respectively. The results, as determined by ANOVA, were statistically significant. As determined by the post test, with the same delay time and injection rate, the attenuation of the artery after biphasic injection (B1) was significantly higher than after monophasic injection (M1).

The mean CT numbers of the vein were 198.5 ± 19.3, 243.2 ± 31.2, 214.8 ± 27.0, and 198.5 ± 18.8 for M1, B1, M2, and B2 protocols, respectively. The results, as determined by ANOVA, were statistically significant. As determined by the post test, regardless of the injection rate, the attenuation of the vein after biphasic injection (B1) was significantly higher than after monophasic injection (M1).

The mean CT numbers of the artery were 198.5 ± 19.3, 243.2 ± 31.2, 214.8 ± 27.0, and 198.5 ± 18.8 for M1, B1, M2, and B2 protocols, respectively. The results, as determined by ANOVA, were statistically significant. As determined by the post test, regardless of the injection rate, the attenuation of the vein after biphasic injection (B1) was significantly higher than after monophasic injection (M1).

Table 2. The Result of the First Step: The Difference of CT Attenuation of Each Tissue between Four Different Injection Protocol Groups

<table>
<thead>
<tr>
<th>Injection Tissue</th>
<th>injection Protocol</th>
<th>p-Value (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid arteries</td>
<td>M1: 189.6 ± 20.8</td>
<td>223.8 ± 35.2</td>
</tr>
<tr>
<td>Internal jugular veins</td>
<td>198.5 ± 19.3</td>
<td>243.2 ± 31.2</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>112.7 ± 12.5</td>
<td>116.6 ± 18.8</td>
</tr>
<tr>
<td>Submandibular glands</td>
<td>121.1 ± 26.0</td>
<td>118.3 ± 20.8</td>
</tr>
<tr>
<td>Sternocleidomastoid muscles</td>
<td>79.0 ± 9.1</td>
<td>77.1 ± 5.8</td>
</tr>
</tbody>
</table>

The data presented are means ± standard deviation.

Note: *CT attenuation is significantly different between the two groups in the post test (Turkey-Kramer test, p < 0.05).

M1 = a high rate monophasic injection group, B1 = a high rate biphasic injection group, M2 = a low rate monophasic injection group, B2 = a low rate biphasic injection with a longer delay time group. ANOVA = analysis of variance.
vascular enhancement (over 150 HU) is no more than 20 seconds, and the examination time with MDCT is very short, close to 12 seconds. However, the time window for optimal vascular enhancement and the shortening of the acquisition time leads to a decreased interval between contrast media administration and image acquisition. This period may be insufficient for the intravascular contrast media to penetrate the tumor and therefore, may result in incomplete tumor enhancement. The incomplete enhancement from a short delay time may result in an inability to identify accurate tumor margins because of poor tumor enhancement (4, 10, 11). The use of a delayed scan at 120 to 180 seconds could improve the conspicuity of a tumor on the post-contrast head and neck CT from the age of conventional CT to MDCT (1, 4, 10). When contrast media were infused with an injection rate of 2 and 3 mL per seconds, interstitial concentrations reached the highest level at 100 to 150 seconds (12). However, the scan delay time within 35 to 70 seconds has been commonly used for the head and neck MDCT (2, 13-15). Therefore, this delay time is too short to sufficiently enhance the solid tissue or the hypovascular tumor. Additional delayed CT scan is one of the solutions for the enhancement of the conspicuity of the tissue. However, since contrast media within the vessels washes out on the delay scan, the radiologist should undergo a comparing between the early scan and the delay scan with inconvenience. Past investigators suggested that digital image fusion of early and delayed scans would combine adequate opacification of vessels and tumors without additional contrast medium administration. However, these methods require two CT scans that double the radiation dose; thus, it is technically difficult to completely match the two images due to the patient’s motion (4). Bartz et al. (10) have suggested that delayed imaging with biphasic injection with a single image acquisition could eliminate the requirement of the

**DISCUSSION**

In the result of the first step of our study, biphasic injection revealed a significantly higher enhancement of the vessel without compromise of the enhancement of tissue compared with the monophasic injection. With biphasic injection in our study, a long delay time (120 seconds) did not decrease the enhancement of vessels, as compared with the use of monophasic injection with a short delay time.

The biphasic injection of contrast media in the head and neck CT has been used to improve the conspicuity of lesions on delayed scans with the use of conventional helical CT (1). As the acquisition time with conventional helical CT was long, a second bolus of contrast media was administrated slowly (0.3-0.5 mL/s) in order to prolong vessel enhancement. To date, as MDCT is quickly becoming the new standard modality for use in head and neck imaging, multiphasic bolus administration of contrast media has become obsolete. With a single bolus administration of contrast media, the time window for optimal enhancement of the vessel is no more than 20 seconds, and the examination time with MDCT is very short, close to 12 seconds. However, the time window for optimal vascular enhancement and the shortening of the acquisition time leads to a decreased interval between contrast media administration and image acquisition. This period may be insufficient for the intravascular contrast media to penetrate the tumor and therefore, may result in incomplete tumor enhancement. The incomplete enhancement from a short delay time may result in an inability to identify accurate tumor margins because of poor tumor enhancement (4, 10, 11). The use of a delayed scan at 120 to 180 seconds could improve the conspicuity of a tumor on the post-contrast head and neck CT from the age of conventional helical CT to MDCT (1, 4, 10). When contrast media were infused with an injection rate of 2 and 3 mL per seconds, interstitial concentrations reached the highest level at 100 to 150 seconds (12). However, the scan delay time within 35 to 70 seconds has been commonly used for the head and neck MDCT (2, 13-15). Therefore, this delay time is too short to sufficiently enhance the solid tissue or the hypovascular tumor. Additional delayed CT scan is one of the solutions for the enhancement of the conspicuity of the tissue. However, since contrast media within the vessels washes out on the delay scan, the radiologist should undergo a comparing between the early scan and the delay scan with inconvenience. Past investigators suggested that digital image fusion of early and delayed scans would combine adequate opacification of vessels and tumors without additional contrast medium administration. However, these methods require two CT scans that double the radiation dose; thus, it is technically difficult to completely match the two images due to the patient’s motion (4). Bartz et al. (10) have suggested that delayed imaging with biphasic injection with a single image acquisition could eliminate the requirement of the

**Table 3. The Result of the Second Step: The Difference of CT Attenuation of Each Tissue between Two Different Injection Protocol Groups**

<table>
<thead>
<tr>
<th>Injection Protocol</th>
<th>M3</th>
<th>B3</th>
<th>p-Value (t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid arteries</td>
<td>177.0 ± 19.8</td>
<td>179.4 ± 22.7</td>
<td>0.72</td>
</tr>
<tr>
<td>Internal jugular veins</td>
<td>182.9 ± 21.2</td>
<td>209.0 ± 34.1</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>108.9 ± 11.2</td>
<td>103.1 ± 9.6</td>
<td>0.08</td>
</tr>
<tr>
<td>Submandibular glands</td>
<td>107.1 ± 28.2</td>
<td>107.4 ± 16.2</td>
<td>0.96</td>
</tr>
<tr>
<td>Sternocleidomastoid muscles</td>
<td>80.4 ± 4.4</td>
<td>78.1 ± 10.4</td>
<td>0.37</td>
</tr>
</tbody>
</table>

The data presented are means ± standard deviation.

Note.—M3 = a low rate monophasic injection with standard volume group, B3 = a low rate biphasic injection with reduced volume group
The injection rate influences the time window of sufficient vessel attenuation. For a spiral CT of the head and neck, using 100 mL of intravenous contrast media with 300 mgI/mL, the optimal injection rate was 2 mL/sec (4). In another study, spiral CT of laryngeal, hypopharyngeal, and oropharyngeal malignancies performed with a single bolus of 90 mL was able to yield excellent tumor enhancement in combination with good vessel enhancement if the flow rate of 1.5 mL/sec is used (5). In contrary to these previous studies, the present study showed that, with monophasic contrast media injection, vessel attenuation with a 2 mL/sec injection rate was not significantly different than that using a 3 mL/sec injection rate. With the same delay time, however, split injection of a contrast bolus was more effective for vessel attenuation elevation than the modulation of the injection rate. As with a previous study on delayed scan, this study was based on the premise that a delayed scan could lead to better conspicuity of a tumor on a CT of the head and neck (Fig. 2).

From the result in the second step of our study, no difference was found in the enhancement of the vessel and tissue between smaller volume of biphasic bolus of contrast media and larger volume of monophasic bolus. Therefore, in patients with decreased kidney function or kidney disease, contrast media may be used in a smaller volume without a decrease of vessel enhancement.

The results of this study led us to the conclusion that biphasic contrast media injection would delay the time window for optimal vessel enhancement without compromising tissue enhancement. Therefore, in the head and neck CT. It would be expected that biphasic injection would be helpful in providing a sufficient scan delay time for tissue contrast concomitant with optimal vessel enhancement.

There are several limitations to this study. First, no pathological lesions were included in the analysis. Therefore, from this study, it cannot be concluded directly whether the biphasic injection will maximize the enhancement of tumor vascularization and involved lymph node or not. However, it can be expected that by biphasic injection and a longer scan time window, the time to penetrate into tumor or lesions will be sufficient. To prove this by using the in-patient comparison, it is necessary that patients should undergo CT examinations twice with different protocol of injection of contrast media. However, this study is difficult to be carried out due to the ethical problem of radiation exposure. A further study that analyzes larger numbers of patients with tumors should be undertaken with a reliable comparison between the injection protocols for tumor enhancement. Second, this study demonstrated the likelihood in
achieving optimal vessel and tissue enhancement by the use of biphasic injection; however, we did not determine an optimal delay time on post-contrast CT with biphasic injection. A specific protocol with defined values could not be set up, but the pattern of biphasic injection could be examined. Finally, biphasic injection may lead to a confusion regarding the vascularity of a tumor. This study is about the conspicuity increase of vessel and tissue for a single CT scan. Therefore, this research may be useful to evaluate cancer staging or lymph node metastasis. In order to evaluate the vascularity of tumor, it would be better to apply the advanced CT protocol, such as perfusion CT or multiphase dynamic CT, than a single CT scan.

In conclusion, compared to monophasic injection, biphasic injection could prolong the scan delay time effectively without a decrease of vessel attenuation or compromising tissue attenuation. In addition, biphasic injection showed similar attenuation with less contrast volume compared to monophasic injection. Thus, optimal enhancement can be acquired even with a reduction of contrast volume in biphasic injection.

REFERENCES

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두경부 다중채널 전산화단층촬영에서 이상형(Biphasic) 조영제 투여의 유용성: 일상형(Monophasic)과의 비교

이준형¹ · 류창우¹ · 김선미¹ · 김의종² · 최우석²

목적: 이 연구는 두경부 multidetector CT (이하 MDCT)에서 이상형 조영제 투여의 효용성을 평가하기 위해 시행되었다.

대상과 방법: 첫 번째 연구에서는 네 군에서 다른 프로토콜을 이용하여 혈관과 조직조영증강을 측정하였다: M1(일상형, 투여속도: 100 mL at 3 mL/초, 스캔시간: 70초); B1(이상형, 100 mL at 3 mL/초, 70초); M2(일상형, 100 mL at 2 mL/초, 70초); and B2(이상형, 100 mL at 2 mL/초, 120초). 이상형 조영제 투여시에는 먼저 50 mL의 조영제를 투여한 후 35초 후에 추가적으로 50 mL의 조영제를 투여하였다. 두 번째 연구에서는 두 군에서 조영제 양과 상을 달리하여 조직조영증강을 측정하였다: M3(일상형, 100 mL at 2 mL/초, 90초) and B3(이상형, 80 mL at 2 mL/초, 90초, 먼저 40 mL의 조영제를 투여한 후 55초 후에 추가적으로 40 mL의 조영제를 투여). 총 여섯 군에서 측정된 혈관과 조직조영증강을 서로 비교하였다.

결과: 동일한 delay time에서는 B1이 M1과 B2보다 혈관조영증강이 높았다(p < 0.05). 긴 delay time에도 불구하고, B2는 M1과 M2에 비해 혈관조영증강의 유의한 차이가 없었다. 각 군 간에 조직조영증강은 차이가 없었다. B3와 M3 간에 혈관과 조직조영증강은 차이가 없었다.

결론: 두경부 MDCT에서 이상형 조영제 주입은 혈관의 조영증강을 증가시키고 적정 스캔시간을 지연시킨다.

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