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Trends in Gadolinium-Based Contrast Agents Use in Radiology Practice: A Retrospective Evaluation

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Abstract

Objective: Contrast refers to the difference in signal strength in magnetic resonance imaging (MRI) that makes it possible to distinguish between different tissues. Contrast agents used in MRI can highlight the differences between tissues and organs, and reveal the differences between normal and pathological tissues. Gadolinium (Gd)-based contrast agents (GBCAs) are widely used in MRI to increase image contrast and enhance image quality.

Methods: GBCA usage data from January 1, 2020 to December 31, 2023 was obtained from hospital medical records. In terms of clinical characteristics, the total number of MRI examinations, the number of MRI examinations performed using GBCA, the number of MRI examinations performed without using GBCA, the type of GBCA used, the number of boxes prescribed, and the contrast volumes used were evaluated.

Results: A total of 167 295 MRI examinations were performed, with 9.8% (16 430/167 295) of these were taken using GBCA. The total number of patients who underwent contrast-enhanced MRI examination is 16 109. While the average age of the patients who underwent MRI examination was 52 years, it was determined that 57% of the patients were female and 43% were male. The number of GBCA boxes prescribed was 2394 in 2020, 3900 boxes in 2021, 4137 boxes in 2022, and 4956 boxes in 2023.

Conclusion: The use of GBCA in MRI increases the reliability and quality of diagnosis, and in our study, its use in our clinic is increasing over the years. To improve patient safety, we recommend that clinicians ensure that their use of GBCA is likely to add clinically meaningful information to imaging by making an individual risk benefit assessment for the patient. Our study will be useful for the radiologists to better understand new trends in contrast-enhanced MRI.

Keywords: MRI, gadolinium, contrast agents

INTRODUCTION

Magnetic resonance imaging (MRI) is a non-invasive and frequently used imaging method that creates diagnostic images using radiofrequency.[1] According to 2023 Organization for Economic Co-operation and Development (OECD) data, the number of MRIs performed per thousand people has the highest value among OECD countries in Türkiye.[2] In MRI, contrast refers to the difference in signal intensity that allows tissues to be separated from each other. Contrast agents applied using various methods (intravenous, oral, etc.) to increase this contrast can reveal the differences between normal and pathological tissues by highlighting the differences between tissues and organs.[3] Gadolinium-based contrast agents (GBCAs) are widely used in MRI to increase image contrast and improve image quality. The first GBCA, gadopentetate dimeglumine, was introduced for clinical use in 1988. The use of GBCAs has expanded the scope of application of MRI and allowed for more specific diagnoses. In the United States, GBCAs are used in 30%-45% of the approximately 40 million MRI examinations performed each year.[4] The use of these compounds is increasing day by day, and studies are continuing to develop new contrast agents.

Gd^{3+} is a heavy metal with 7 unpaired electrons and is highly toxic in its free ionic form, and can disrupt calcium-mediated signaling pathways. Therefore, in order to form a stable complex, it must be bound with a suitable ligand. All GBCAs consist of a Gd^{3+} with paramagnetic properties tightly bound to a chelating ligand. They are divided into macrocyclic/linear and ionic/nonionic agents according to ligand structure (Table 1).[4] Macrocyclic GBCAs have higher stability.[5] Most GBCAs are excreted renally. The choice of GBCA in clinical practice often depends on several variables, such as local protocols, physician expertise, patient expectations, financial constraints, molecule stability, and adverse effects.[6] Gadolinium-based contrast agents are administered intravenously. The approved standard dose of GBCA during a single imaging session is 0.1 mmol/kg.[7]

Gadolinium-based contrast agents are generally considered safe. However, following their application, mild adverse reactions such as nausea, vomiting, pain at the injection site, headache, and dizziness may occur. Additionally, disorders such as hypersensitivity reactions, nephrogenic systemic fibrosis, and gadolinium deposition disease have been reported. Gadolinium may accumulate in the brain and extracranial organs (bone, kidney,

Table 1. Gadolinium-Based Contrast Agents

Active Ingredient	Trade Name	Structure
Gadoterate meglumine (Gd-DOTA)	Dotarem (withdrawn from the Turkish market) Clariscan	Macrocyclic ionic
Gadobutrol (Gd-DO3A-butrol)	Gadovist	Macrocyclic nonionic
Gadodiamide (Gd-DTPA-BMA)	Omniscan (withdrawn from the Turkish market)	Linear nonionic
Gadopentetate dimeglumine (Gd-DTPA)	Magnevist Emaray	Linear ionic
Gadobenat dimeglumine (Gd-BOPTA)	MultiHance (withdrawn from the Turkish market)	Linear ionic
Gadoxetic acid disodium	Primovist	Linear ionic
Gadoversetamide (Gd-DTPA-BMEA)	Optimark	Linear nonionic

skin, and lymph nodes). The health effects of these accumulations have not yet been fully determined. More research and long-term follow-up are needed.[1,4] Regarding the prevention of gadolinium accumulation, especially in the brain, it has been recommended that GBCAs should be used only when medically necessary, the recommended dose should not be exceeded, and repeated applications should be avoided except for clinical indications.[8] In addition, in recent years, there have been suspicions that these substances may have genotoxic and cytotoxic effects, and studies on this subject are continuing.[9] It seems that their use should be approached with caution in clinical applications. During their use, it is necessary to evaluate the individual risk-benefit for the patient to ensure that there is a high probability of adding clinically meaningful information to the imaging.

Like all other biomedical products, the use of GBCA carries risks for patient health. There are studies in the literature evaluating the effectiveness, safety, and use of GBCAs. However, there are no studies reflecting real-life clinical data regarding the use of GBCAs in Türkiye. Our aim in this study is to determine the usage trends of GBCAs, which are frequently used in practice, in radiology clinics between 2020 and 2023. The findings we obtain from this study will guide the use of GBCAs.

MATERIAL AND METHODS

This study was approved by the Erzincan Mengücek Gazi Training and Research Hospital institutional ethics committee (Number: 2024-13/3, Session: 3, Date: 13.03.2024) and the ethics committee has waived the need for informed consent due to the methodology of the study.

Study Design

Our study was conducted retrospectively in the radiology clinic of a tertiary hospital. Gadolinium-based contrast agent usage data from January 1, 2020 to December 31, 2023 was obtained from hospital medical records.

Evaluated Variables

The research included patients from all age groups. Age and gender data were obtained for demographic characteristics. In terms of clinical characteristics, the total number of MRI examinations, the number of MRI examinations performed using GBCA, the number of MRI examinations performed without using GBCA, the type of GBCA used, the number of boxes prescribed, and the contrast volumes used were evaluated.

Statistical Analysis

Data were evaluated with the SPSS 20 program (IBM SPSS Corp.; Armonk, NY, USA). The Kolmogorov–Smirnov test was applied to determine whether the numerical values were normally distributed. Normally distributed data are presented as mean ± standard deviation. Categorical data are expressed as number (n) and percentage (%).

RESULTS

Magnetic resonance imaging examinations were performed on a total of 16 109 patients between January 1, 2020 and December 31, 2023. While the average age of the patients who underwent MRI examinations was 52, it was determined that 57% of the patients were female and 43% were male.

A total of 167 295 MRI examinations were performed between January 1, 2020 and December 31, 2023. Of these, 9.8% (16 430/167 295) were conducted using GBCA. The number and ratio of contrast-enhanced and non-contrast MRI examinations by year are presented in detail in Table 2. The number of contrast-enhanced examinations and patients by year is presented in detail in Table 3.

Of the 2394 boxes of GBCA prescribed in 2020, 7% were Gadodiamide (Omniscan), 37% were Gadoterate meglumine (Dotarem), and 56% were Gadobutrol (Gadovist). Of the 3900 boxes of GBCA prescribed in 2021, 25% were Gadoterate meglumine (Clariscan) and 75% were

MAIN POINTS

- Gadolinium (Gd)-based contrast agents (GBCAs) are widely used in MRI to increase image contrast and improve image quality.
- A total of 167 295 MRI examinations were performed in our clinic between January 1, 2020 and December 31, 2023, and 9.8% (16 430/167 295) of them were performed using GBCA.
- The total number of patients who underwent contrast-enhanced MRI examinations was 16 109. While the average age of the patients who underwent MRI examinations was 52, it was determined that 57% of the patients were female and 43% were male.
- The use of GBCA in MRI increases the reliability and quality of diagnosis, and in our study, its use in our clinic has been increasing over the years. Our study will be useful for radiologists to better understand new trends in contrast-enhanced magnetic resonance.

Table 2. Number of MRI Examinations by Years

Year	Contrast-enhanced MRI Examination (%)	Non-contrast MRI Examination (%)	Total Examination (%)
2020	3545 (8.5)	38 223 (91.5)	41 768 (100)
2021	4479 (10)	40 275 (90)	44 754 (100)
2022	3842 (7.6)	46 448 (92.4)	50 290 (100)
2023	4564 (14.9)	25 919 (85.1)	30 483 (100)
Total	16 430 (9.8)	150 865 (90.2)	167 295 (100)

MRI, magnetic resonance imaging.

Table 3. Number of Contrast Examinations and Number of Patients MRI Examination by Years

Year	Contrast-enhanced MRI Examination (n)	Patient (n)
2020	3545	3462
2021	4479	4398
2022	3842	3770
2023	4564	4479
Total	16.430	16.109

MRI, magnetic resonance imaging.

Gadobutrol (Gadovist). Of the 4137 boxes of GBCA prescribed in 2022, 25% were Gadoterate meglumine (Clariscan), 8% were Gadoterate meglumine (Dotarem), and 67% were Gadobutrol (Gadovist). In 2023, 20% of the total 4956 boxes of GBCA prescribed were Gadoterate meglumine (Clariscan) and 80% were Gadobutrol (Gadovist).

DISCUSSION

Macrocyclic ionic/nonionic and linear nonionic GBCAs were preferred in GBCA prescriptions. Guerbet Pharmaceuticals announced that Dotarem was withdrawn from the Turkish market on November 22, 2022. It has been observed that Dotarem had been preferred in MRI contrast agent prescriptions until that date.

The European Medicines Agency (EMA) suspended the license or restricted the use of some linear compounds, and later the US Food and Drug Administration announced that linear agents accumulate more in the brain than macrocyclic agents.[10,11] In 2017, the EMA allowed the use of the linear agents gadoxetic acid and gadobenate dimeglumine for limited indications (liver imaging), while suspending the use license of gadodiamide, gadopentate dimeglumine, and gadoversetamide. It has been reported that macrocyclic agents can continue to be used at the lowest dose that will provide optimal contrast and will not reduce diagnostic accuracy.[10,12]

In Europe, GBCAs are used properly for a variety of indications, demonstrating a significant improvement in diagnostic confidence. Following GBCA usage, it was established that GBCAs have a favorable safety profile, with findings for each agent employed being comparable (Clariscan, Dotarem (gadoteric acid), Gadovist (gadobutrol), and ProHance (gadoteridol)).[13]

In a European-based, multicenter, prospective study evaluating the use patterns of macrocyclic GBCAs in MRI of the central nervous system, gadoterate meglumine (Clariscan) was used in 66% (503) of cases, gadoterate meglumine (Dotarem) was used in 20% (160), gadobutrol (Gadovist) was used in 13% (97), and gadoteridol (ProHance) was used in 1% of the examinations.[6]

In a study evaluating the clinical use of the macrocyclic gadolinium-based contrast agent gadoterate meglumine (Clariscan) in 6 university hospitals in Korea, 1376 patients were included in the study during the evaluation period. The average volume of Clariscan used was 0.26 mL/kg. When MRI examinations were classified according to body regions, 69% included the nervous system, 13.6% the musculoskeletal system, and 4.9% the reproductive system. There were 14 adverse events in 10 patients, and Clariscan was generally well tolerated.[13]

In a prospective multicenter study in Europe, 2118 patients from 8 centers in 5 European countries were evaluated. Gadoterate meglumine (Clariscan) was used in 71.4% of the patients, gadoterate meglumine (Dotarem) in 16.8%, gadobutrol (Gadovist) in 11.2%, and gadoteridol (ProHance) in 0.6%. Most MRI examinations were performed for indications related to the central nervous system (46.2%). Adverse events were observed in 4 patients (0.19%).[14]

In conclusion, the use of GBCAs in MRI increases the reliability and quality of diagnosis, and in our study, its use in our clinic has been increasing over the years. In a non-comparative analysis with previous studies, no significant diagnostic difference was observed between GBCAs used in MRI in our clinic. To enhance patient safety, we advise clinicians to restrict the amount of GBCA administered, enhance patient education during GBCA administration, meticulously maintain institutional records of the volume and frequency of agents administered, and implement institutional outcome reviews and monitoring to detect gadolinium accumulation in patients receiving multiple doses. Our study will be useful for radiologists to better understand new trends in contrast-enhanced magnetic resonance.

Ethics Committee Approval: This study was approved by the Erzincan Mengücek Gazi Training and Research Hospital institutional ethics committee (Number: 2024-13/3, Session: 3, Date: 13.03.2024)

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